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SER. II, VOL. 22 *February 1960* NO. 4

TRANSACTIONS
OF
THE NEW YORK ACADEMY OF SCIENCES

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Transactions of The New York Academy of Sciences, Series II, Volume 22, No. 4
February 1960

Second-class postage paid at New York, N. Y. This publication is distributed to members and is published monthly from November to June, inclusive, by The New York Academy of Sciences, 2 East Sixty-third Street, New York 21, N. Y.

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SECTION OF GEOLOGICAL SCIENCES

GEOLOGICAL PROBLEMS IN THE CONSTRUCTION OF DAMS*

Kemble Widmer

New Jersey Department of Conservation and Economic Development, Trenton, N.J.

The December 24, 1959 issue of *Engineering News Record* contains an editorial on the recent failure of the Malpasset Dam near Fréjus, France. After praising the ability of André Coyne as designer, it considers it "highly unlikely that he failed to give careful consideration to the foundation conditions" because there has been "emphatic recognition, in professional dissertations, of the peculiar importance of foundation stability to the safety of thin arch dams." The editorial goes on to conclude that the engineering profession is perhaps "least proficient in predicting foundation behavior," that this disaster may "highlight the need for intensifying engineering emphasis on geology and foundation exploration," that the geological study may not have "reflected the best that the art in its present state can offer," and that the foundation exploration was perhaps not "thorough enough to support the geological opinion."

This editorial only echoes the statements made by F. L. Ransome and C. P. Berkey in 1929 after the failure of the St. Francis Dam near Los Angeles, Calif. Ransome said: "The plain lesson of the disaster is that engineers, no matter how extensive their experience in the building of dams or how skillful in the design of such structures, cannot safely dispense with the knowledge of the character and structure of the adjacent rocks, such as only an expert and thorough geological examination can provide" (Ransome, 1929).

Also in 1929, in discussing the responsibilities of the geologist in engineering projects, C. P. Berkey said: "An impractical project must not be begun; all reasonable doubt of its feasibility must be removed. Serious questions as to the behavior of the ground must be settled before construction begins. Dams must stand. Not all of them do, and there are all degrees of uncertainty about them. Reservoirs must hold water. Not all of them do, and there are many ways by which water may be lost. The work must be done safely as a construction job. Not all of them are, and there are many sources of danger. The whole structure must be permanent and the work has a right to be done within the original estimates. Not all of them are, and there are many reasons for their failure or excess cost, most of them geologic or of geologic dependence.

*This paper, illustrated with slides, was presented at a meeting of the Section on January 4, 1960.

"If these requirements are not attained, it is generally either the fault of the geologist advisor, who ought to see the difficulties and dangers and impossibilities in advance, or it is the fault of the chief engineer who presumes too much on his own acquaintance with geologic matters and has failed to procure the necessary advice. The time has gone by for anyone to assume personal competence in every one of the fields that may require research ability on an engineering project; and the time has gone by for such work to be done by an untrained or unskilled man" (Berkey, 1929).

Thus we find that after thirty years many engineers still consider geology an art and apparently are inclined to assume not only that all geologists as equally able practitioners of their art, if such it be, but also that there is such a thing as an engineering geologist. Both assumptions could hardly be further from the truth: first, because there are probably as many fields of specialization in geology as there are in engineering, and not in civil engineering alone; and, second, because there is no such thing as an engineering geologist – professional cards and letterheads notwithstanding. As Edward B. Burwell and George D. Roberts so aptly put it in the opening chapter of *Application of Geology to Engineering Practice* (the Berkey volume, 1950): "Engineering Geology is not a branch of the science of geology; it is the application of all of the branches of the science to the practical problems of engineering. Physiography, historical geology, stratigraphy, structural geology, petrography, economic geology, ground-water hydrology, and even paleontology – all these divisions of the science have important applications in civil engineering " (Paige, 1950).

There are all degrees and shades of competence and training in the field of engineering geology. Some are engineers with additional training in geology; others are geologists with training as engineers; still others may have had very little formal training, but a broad and varied experience backed by avid reading on case histories and general geology pertinent to the engineering problems. The most important requirement is that the engineer or geologist have sufficient geologic knowledge to know what field or fields of geology may be applied to the problem to obtain the necessary answers. Nature abhors regularity and precise classification, and the geologist therefore must recognize the range of conditions that may be present, not only with respect to the geologic materials, but also with respect to the geologic structure and history of the region in which the engineering project is to be constructed.

Before proceeding with an examination of specific examples or the general problems incident to applying geologic knowledge to the construction of dams, it should be emphasized that most dams stand, most reservoirs hold water, and that geologic and engineering studies on most projects are adequate and complete. Like the train wreck or the juvenile delinquent, the failure of a dam is a choice news story, while good opera-

tion, good behavior, or a job well done has little news value.

Successful dams of large size were built in Egypt and in the Near East in the dawn of history. The dam built by Menes, first king of Egypt, 12 miles north of Memphis, Egypt, about 4000 B.C., supplied water to an irrigation project for 4,500 years until maintenance was discontinued. In the past century, also, the number of dams that have failed, never a large percentage of the total number, has decreased.

Of all the projects of heavy construction in engineering, dams and reservoirs are probably the most interesting to the public. In cost, in the magnitude of materials moved, in their effect upon the region, even a small project staggers the imagination and is beyond the experience of most citizens. As engineering projects, dams and reservoirs probably do more to upset the natural conditions within and adjacent to the project than do other types of construction. Not only is the natural process of stream erosion completely changed within the reservoir area but, what is perhaps less obvious, the natural balance of the process is affected upstream from the reservoir and, of course more obviously, downstream from the dam itself. Ground water conditions that all too often may be ignored because they are, so to speak, "out of sight, out of mind" may be affected profoundly. Water will not run uphill, except under pressure, but a dam or reservoir may provide that pressure.

Perhaps it should be noted also that many of today's leading engineering geologists have attained much of their fame because of their association with reservoir projects.

The Bureau of Geology and Topography of the New Jersey Department of Conservation and Economic Development in the past year has been directly or indirectly concerned with the geologic problems of four dam and reservoir projects in the state. Previous to 1959, the bureau has been concerned (chiefly as a source of regional geologic data) with these and other proposed projects. The wide range of geologic conditions within the state – four physiographic provinces and rocks of every geologic period except Carboniferous, Permian, and Jurassic – presents a wide and complex variety of geologic problems in the four projects (FIGURES 1 and 2).

The first project at the moment must remain unidentified, but is a project in which the dam and reservoir are underlain by a hard, impermeable quartzite. Here the main problem is one of determining the detailed geologic structure with particular reference to the faults and jointing of the gently folded formation that is about 1500 feet thick. The bureau has been assisting the engineers and geologic consultants in determining the details of spacing, continuity, and direction of faults and joints, since these would be potential zones of leakage from a reservoir several hundred feet above the adjacent valleys.

The Charlotteburg Reservoir is the newest of the system of six reservoirs in the Pequannock Watershed of Newark and is the second of the

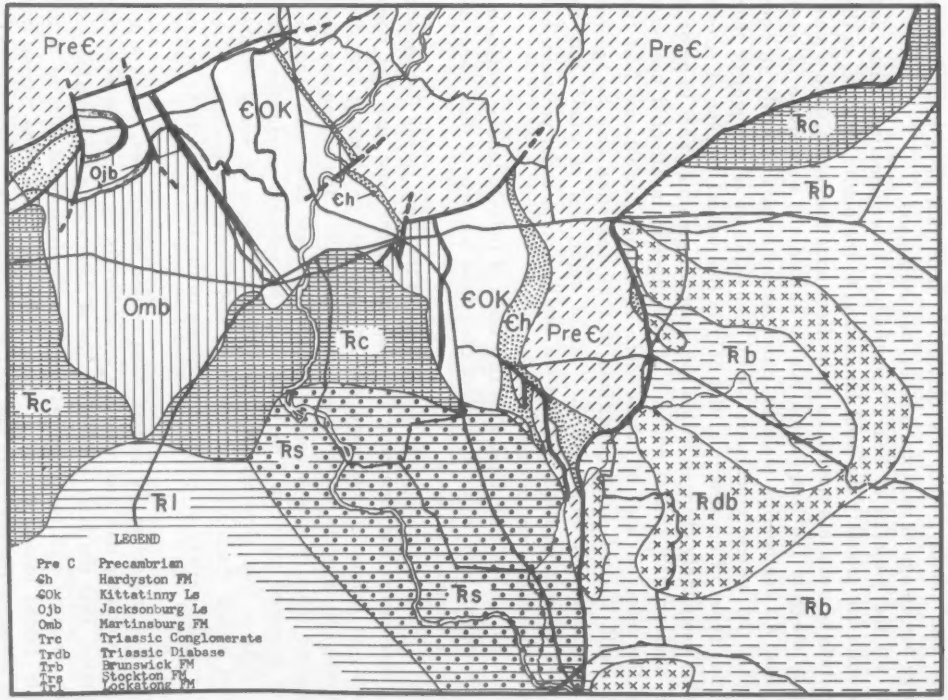


FIGURE 1. One-mile-to-the-inch generalized enlargement of the state geologic map in the Spruce Run-Round Valley area. Round Valley is within the diabase ring on the right side of the map and Spruce Run Reservoir is generally underlain by the Kittatinny limestone in the upper left corner.

Run-Round Valley area. Round Valley is within the diabase ring on the right side of the map and Spruce Run Reservoir is generally underlain by the Kittatinny limestone in the upper left corner.

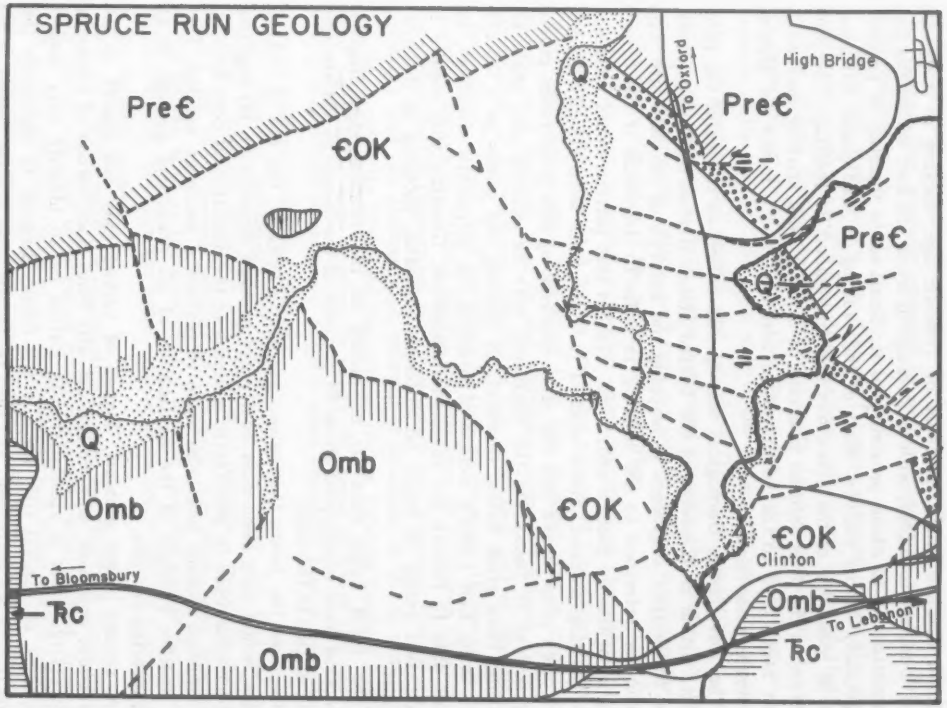


FIGURE 2. Detailed geologic map of the Spruce Run Reservoir area showing the major faults, the contacts, the major formations, and the recent stream gravels.

four projects. It will be the first of the newer reservoirs in New Jersey in operation, since more than 50 per cent of construction is completed.

Although some of the reservoir is underlain by Paleozoic sediments, the dam foundation is entirely within Precambrian gneisses intensely folded and metamorphosed. Intruded into these rocks are at least 9 fine-grained diabase dikes, probably of Triassic age, varying in thickness from 2 inches to 6 feet, with an average of about 2½ feet within the dam foundation or in close proximity to it. Small-scale faulting is present, especially in the valleys. Most of the faulting is prediabase intrusion, but at least one of the dikes has been displaced by faulting. The joint system in the Precambrian consists of 3 major sets striking northwest, with steep dips to the southwest or northeast and a fourth set dipping moderately northeast.

The New Jersey Geological Survey was called on to assist the geologist, Arthur B. Cleaves, of the United States Bureau of Public Roads, and the project engineers in mapping the bedrock of the dam site with particular reference to the jointing in order to determine if there were any recognizable pattern and, if so, whether this pattern would influence the grouting program. Since most of the joint sets were steeply dipping and often were thrown into the other quadrant of dip, joint roses proved impractical in furnishing the engineers with an azimuth and angle for drilling their grout holes. However, by plotting the joints on a Schmidt net, using Kurt Lowe's method of counting out petrofabric diagrams, we were able to furnish the required information. Grouting will require at least two series of holes on different azimuths, inclined at different angles.

The grout holes thus far completed on the recommended diagonal direction have intercepted about 85 per cent of the joints as satisfactory high angles to the core.

Because the joints themselves are nearly vertical, the use of vertical holes would have been most costly and perhaps impractical. By applying a technique used in petrofabric analysis to the direction of core drilling, a minimum footage has been made to perform a maximum service. This is another example of the application of all phases of geology to an engineering problem.

A second minor problem, lenses of varved clay and gravel in the northwest abutment, was worked out with Paul MacClintock of Princeton University. Here a specialist was called on to identify very similar deposits of glacial till, make a till fabric diagram to determine the direction of ice movement, and then reconstruct the glacial history of the area. With this information at hand, selected core borings were checked again to verify this sequence of events to determine whether any buried Ice Age stream channels of sand and gravel might exist through the northeastern reservoir rim. This problem points up the occasional need to obtain the service of a specialist in a particular field of geology

and also the importance of reconstructing the full history of geologic events in the area of a major engineering project.

The third project is that now under investigation by the Department of Conservation and Economic Development at Round Valley. The Bureau of Geology assisted the North Jersey District Water Supply Commission in the original geologic investigation of preliminary core borings. In 1958 the bureau was actively engaged in regional geologic studies that are still continuing.

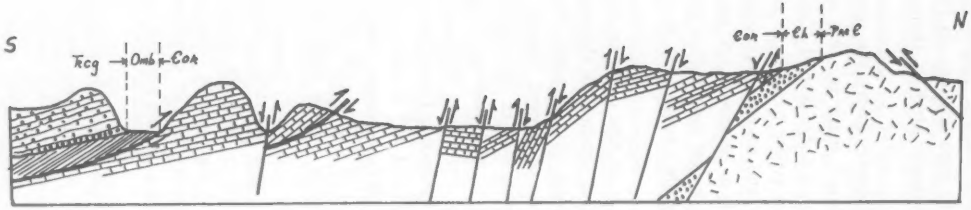
Cushetunk Mountain, a ring dike of Triassic diabase, forms the north, east, and south rims of a 55-billion-gallon "off-river" reservoir that will occupy Round Valley, in Hunterdon County (FIGURE 3). Round Valley is underlain by Triassic shale that has a dip and strike similar to that outside of the valley. The west side of the valley and reservoir is underlain by Precambrian gneiss and infaulted Cambrian quartzite. A major branch of a regional fault runs northward through the south dam site, branches within the valley, and runs out of the valley northward as two faults under the sites of the north dam and dike.

The contacts, jointing, and other characteristics of the diabase mass are concealed by the thick woods and talus slopes of Cushetunk Mountain. Older geologic reports suggested that the diabase was a cone sheet related to a diabase plug in the northwest corner of Round Valley. A broadening of the diabase outcrop at the southwest end of the outcrop "horseshoe" would lend credence to this assumption. However, a geophysical survey by William Bonini and students of Princeton University, completed for the Department of Conservation and Economic Development, indicates that the diabase dips outward at an angle of 60° or more, thus forming a ring dike. Core drilling on the rim on 100-foot centers has not been sufficiently deep or close to verify the angle of dip of the contact. A ring dike would seem to be slightly more desirable than a cone sheet if there were any potential leakage.

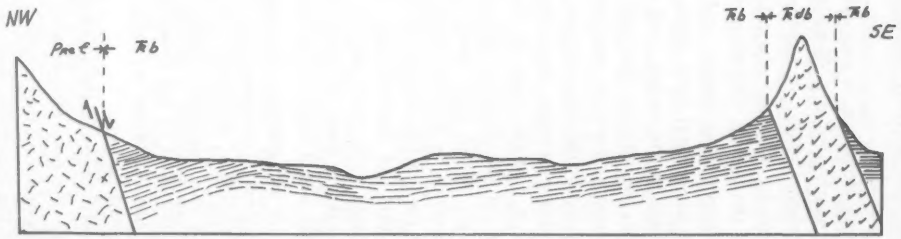
The resident geologists for the design engineers for this project – Porter, Urquhart, McCreary and O'Brien of Newark – have the responsibility for the detailed geology of the area, but have been assisted by the bureau staff in the examination of core samples and in structural interpretations, because the local details of structure are so much a part of the regional pattern.

In the early stages of the examination of core samples from the northern fault areas, one core effervesced freely when acid was applied. Immediately it was assumed that a block of Kittatinny limestone, which normally lies above the quartzite, had been dragged down into the fault zone. A petrographic thin section solved the problem, as it showed badly fractured gneiss rehealed by abundant calcite.

The fourth project is the 11-billion-gallon "on stream" reservoir on Spruce Run just north of Clinton, N. J., about 5 miles west of Round Valley (FIGURE 3). It became apparent in May 1959 that the geologic



SPRUCE RUN



ROUND VALLEY

FIGURE 3. General north-south cross section throughout the Spruce Run Reservoir along the general line of Spruce Run and the South Branch of the Raritan River. The lower section is a north-west south-east section through Round Valley more or less parallel to the road running down the center of the valley shown on FIGURE 1.

investigation of the site needed re-enforcement. Salvatore A. Bontempo of the Department of Conservation and Economic Development therefore assigned the Bureau of Geology to participate actively in the geologic investigation. Previous to this decision, the bureau had been concerned only with the regional geologic picture and the logging of core from the boring program.

The dam, spillway, about one half of the reservoir, and the entire east rim of the reservoir are underlain by Ordovician Kittatinny limestone. The west dike, one half of the more easterly dike, and the western part of the reservoir are underlain by late Ordovician Martinsburg shale. Both formations are highly faulted and, in some places, the limestone is quite highly folded. Precambrian gneiss is in fault contact with both limestone and shale on the north. Gneiss and Cambrian quartzite are found east of the reservoir. More or less east-west faults affect the gneiss, the Hardyston quartzite, and the limestone in the eastern part of the reservoir.

In the early stages of the development of the geologic structure, the topographic maps were examined for "linears" that were checked in the field and then on air photos. Where the Hardyston quartzite has been offset by the above-mentioned faults and where major structures crossed several rock types this method proved speedy and effective.

Seismic and resistivity surveys were also made to determine the depth to sound rock. Later information from core borings confirmed, in general, the interpretations made of the geophysical data. It should be noted that these interpretations were difficult to make and have not always been successful. These studies were greatly expedited by running the early tests between two parallel lines of drill holes.

In the area underlain by shale, determination of the geologic structure required detailed stratigraphic work and field examination of a large area adjacent to the reservoir. Once a more or less normal section had been determined, individual shale types and marker beds were traced into the reservoir area. The shale was found to be overthrust, and certain areas that seemed inconsistent were found to be limestone beds in the normal shale sequence, not fault slices of the underlying Kittatinny limestone.

Throughout the study a great deal of attention was paid to the static water level as the core holes were put down. Well and spring information was gathered, and ground water level data were continually examined with reference to rock type, structure, and the possible significance or cause of areas of low or changing ground water levels. Several problems are still unsolved in this area of investigation.

The preparation of several projections and cross sections indicates that the present topographic surface in the area has less relief than did the surface developed in early Triassic times on the limestone and shale upon which the Triassic fanglomerates were deposited before the Paleozoic rocks were exhumed by the present erosion cycle. It was

east section through Roseta Valley more or less parallel to the road running down the center of the valley shown on FIGURE 1.

assumed that an older set of solution cavities than those formed by the present cycle of erosion had been developed. This assumption was confirmed by brown clots in the drill cores that turned out to be fine silt cemented by calcite.

Work continues on the detailed geology of the Spruce Run area. In addition to core borings and open trenching, the geologic investigation has required the application of both regional and detailed structural geology, stratigraphy, petrography, petrology, geophysics, air photo interpretation, paleontology (some microfossils were found in the cores), ground water geology, geomorphology, historical geology, and Pleistocene geology.

These four cases illustrate the wide range of geologic problems that may be encountered in major engineering projects in New Jersey. They also demonstrate that engineering geology is the application of all phases of geology to engineering problems and not, as is often assumed, a branch of geology.

References

RANSOME, F. L. 1929. Geology of the St. Francis dam site. Econ. Geol. :553.

BERKEY, C. P. 1929. Responsibilities of the geologist in engineering projects. A. I. M. E. Tech. Publ. 215.

PAIGE, S. (Ed.). 1959. The geologist in the engineering organization. *In* Application of Geology to Engineering Practice. :2. Geol. Soc. Am. New York, N. Y.

NUCLEI FORMATION AND CRYSTAL GROWTH IN MINERALIZING TISSUES*

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Mineralization is widespread in lower as well as vertebrate organisms. In lower animals mineralized tissues are external, composed predominantly of calcium carbonate. In vertebrates they are internal, consisting predominantly of calcium phosphate with some carbonate. This discussion will be confined to the mineralization of bones and teeth in vertebrates. However, the general principles probably apply also to mineralization in invertebrates.

Bone contains 65 to 70 per cent mineral salts and 30 to 35 per cent organic matter.[1] Of the organic fraction, approximately 95 per cent is collagen. X-ray diffraction studies define the mineral fraction as apatite, organized as illustrated in FIGURE 1. The crystals are oriented parallel to the collagen fibers.[2-4] The composition can be expressed empirically as $[Ca_3(PO_4)_2]n \cdot CaCO_3$, in which some carbonate is replaceable by citrate and fluoride, and some calcium is replaceable by magnesium, sodium, strontium, lead, and hydrogen.[5] Most variations in composition occur in the adsorption layer (G. Carlström, personal communication).

Nuclei Formation

Nuclei formation, the first step in the mineralizing process, may be described as the emergence from a metastable phase of the first fragments of a new phase capable of growth into larger aggregates. In bone we are referring to the emergence of a solid from solution. Better understanding of the mineralization of tissues awaits the future development of a general theory of nucleation of a solid from solution.

According to R. Ginell (personal communication), of the many possible associations of particles, only certain configurations are capable of acting as prenuclei of crystal growth, and their formation requires activation energy.[6] Best[7] developed an equation for the formation of calcium phosphate microaggregates in the absence of nucleating catalysts by a bimolecular reaction. However, it is inadequate to define the nucleation of bone mineral.

*This paper, illustrated with slides, was presented at a meeting of the Section on January 5, 1960. The work described was supported in part by the United States Air Force under contract AF 41(657)-229 monitored by the School of Aviation Medicine, USAF, Randolph AFB, Texas; the National Institute of Dental Research, Public Health Service, Grant D-55, Bethesda, Md.; and the Office of Naval Research Project NR 105-025, Washington, D.C. Reproduction in whole or in part is permitted for any purpose of the United States government.

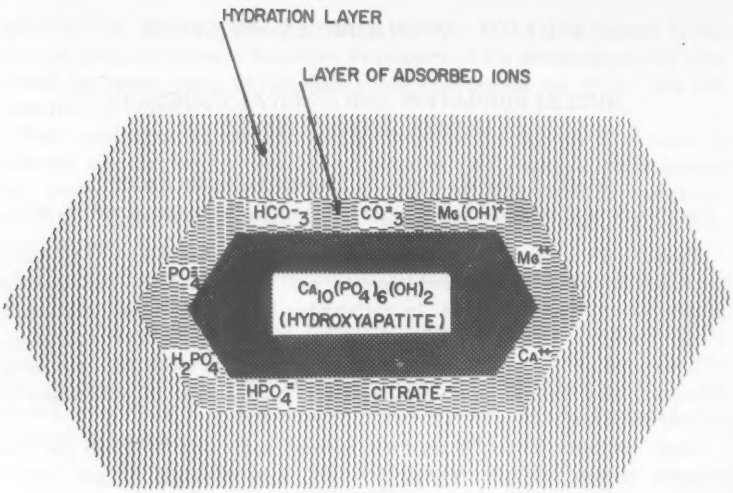

FIGURE 1. Bone crystal in body fluid. Schematic diagram.

The minimal chemical potential, which may be expressed for bone mineral as $[A_{Ca}{}^{++}][A_{HPO_4}{}^{=}]$, required to form nuclei for hydroxyapatite crystals is unknown. For nucleation the concentration of the reactants must equal or exceed the chemical potential (μ) of the nuclei themselves. In the nucleating system, $\mu_{solution} > \mu_{nuclei} > \mu_{microcrystal\ surface}$ $\mu_{macrocrystal\ surface}$. If μ for nuclei formation is greater than μ of the body fluids, then the nucleating mechanism must increase the chemical potential in the fluid before catalyzing nucleation. If μ of the nuclei is below μ of the body fluids, then the minimal task of the nucleating mechanism is to form nuclei (FIGURE 2). If μ for nucleation is close to the solubility product of $CaHPO_4 \cdot 2H_2O$, the task of the nucleating mechanism is concentration of the reactants as well as formation of nuclei, since this product exceeds the concentrations of calcium and phosphate in extracellular fluid. Since the body fluids are supersaturated with respect to hydroxyapatite, it has been suggested that the only task of the nucleating mechanism is the formation of nuclei, via epitaxis.[8] However, it is kinetically unlikely that a lattice unit of 18 ions, $Ca_{10}(PO_4)_6(OH)_2$, could be formed in one interaction.

Mineralizing tissues probably utilize the following methods for nucleation: first, increasing the concentration of ions and, second, reducing the required $[A_{Ca}{}^{++}][A_{HPO_4}{}^{=}]$ for the formation of nuclei by means of a catalyst (FIGURE 2). Earlier theories proposed that the critical step in the calcifying mechanism is concentration of phosphate ions until the Ca × P product is sufficiently high for spontaneous precipitation. This is the essence of Robison's phosphatase theories,[9,10] expanded

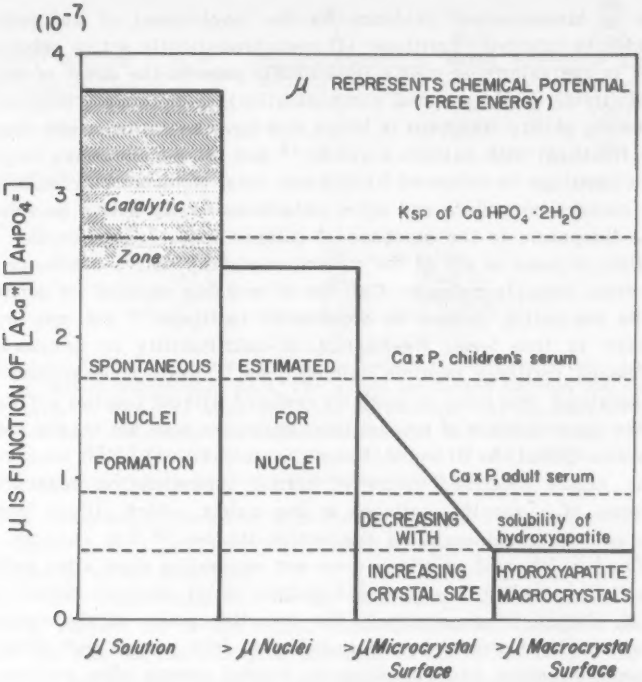

FIGURE 2. Ca × P product at various stages of nuclei formation and crystal growth.

by Gutman to include phosphorylative glycogenolysis.[11,12] The demonstration of ATP in calcifying cartilage supports the view that it is directly involved in nuclei formation by splitting, providing phosphate and energy.[13] However, phosphatase, ATP, and the glycolytic enzymes are not confined to mineralizing tissues, whereas the sites of mineralization are defined exactly.

Two findings led to the modern concept of mineralization: (1) reconstituted acid-soluble collagen as well as acid-insoluble collagen (cross-linked) induce nucleation,[14-16] suggesting that this protein is the catalyst of nuclei formation in bone; and (2) nuclei in their first stages of growth (produced in preosseous cartilage) will continue to grow in a histologically valid manner after destruction of the nucleating mechanism.[17] In the tissues the nucleating collagen probably is a complex with a mucopolysaccharide or mucoprotein. To date, calcifiability in demineralized bone seems to be restored best after treatment with mucopolysaccharides; the restored mineralization is confined to the usual calcifying sites (Sobel, A. E, and M. Burger, in preparation). In addition,

there is histochemical evidence for the involvement of mucopolysaccharides in calcifying cartilage: (1) metachromatically active substances occur in the calcifying matrix immediately prior to the onset of calcification (Irving, J. T., personal communication); (2) both metachromasy and nucleating ability disappear in bones that have been frozen and reappear after treatment with calcium chloride;[18] and (3) metachromasy in preosseous cartilage is enhanced by calcium ions. Metachromasy induced by pure chondroitin sulfate and other metachromatically active polyelectrolytes disappears in the presence of calcium ions.[19] This implies combination of some or all of the metachromatically active substance with a protein, probably collagen. Calcium is probably required for activation of the nucleating system in preosseous cartilage,[20] but may not be required in true bone. Restoration of calcifiability in demineralized preosseous cartilage requires calcium ions,[20] while mineralizability of demineralized true bone is partially restored without calcium activation, and the mineralization of reconstituted collagens does not require calcium activation (Sobel, A. E. and M. Burger, in preparation).[14-16]

The highly localized nature of normal mineralization suggests the presence of a specific collagen in the matrix, which differs from the collagens in nonmineralizing connective tissues.[21] For example, nonossifying epiphyseal cartilage does not mineralize even after calcifiability is restored in demineralized rachitic tibial sections (Sobel, A. E. and M. Burger, in preparation). The selective action of the nucleating system is demonstrated by its inability to form nuclei with strontium, although strontium can contribute to crystal growth after calcium-containing nuclei are produced.[22]

The active centers of the nucleating molecule probably contain two ion-capturing sites. This view is supported by the transformation of nonstriated collagen fibers to collagen striated with a periodicity of 640 Å by either calcium or phosphate ions.[23] The cation-linked inhibition of calcification *in vitro* by fluoride, cyanide, and iodoacetate ions also suggests two sites.[24-26]

Nuclei formation in bone: a proposed mechanism. The active form of the nucleating center, probably between collagen protofibrils, is brought out by interaction with a mucopolysaccharide or mucoprotein and probably requires calcium ions in preosseous cartilage. These centers are selective in that they will not catalyze nucleation with strontium ions. To increase metastability, calcium and phosphate ions are probably concentrated. They are then captured at two sites, or a prenucleus may be captured, subsequently undergoing transformation to nuclei *in situ*, by means of a lock-and-key mechanism[21] (FIGURE 3). The energy for nuclei formation is probably provided by a specialized mechanism.

Components of the nucleating system, present in the calcifying matrix, which may provide energy and/or concentrate the ionic species are: (1) phosphatase; (2) the enzymes of phosphorylative glycogenolysis;

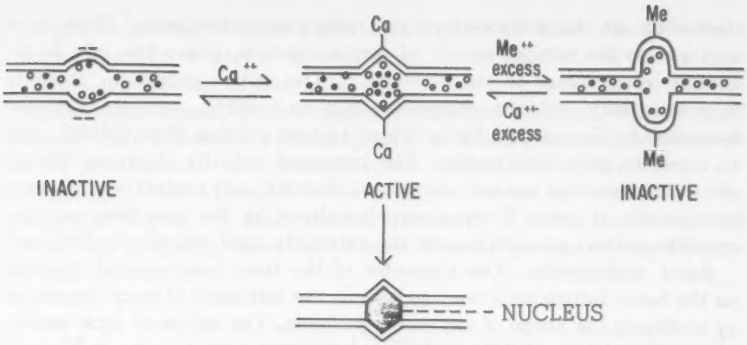

FIGURE 3. Model of nuclei-forming mechanism including reversible inactivation by calcium-substituting ions. The nuclei are formed between the collagen protofibrils at selective sites activated by calcium. The complete system is activated by a mucoprotein or mucopolysaccharide, and utilizes energy such as is obtained from ATP, UTP, glycolytic, and/or citric acid cycles. The actual mechanism must be visualized as a three-dimensional process.

(3) the enzymes of the citric acid cycle; and (4) energizing compounds such as ATP and UTP. In addition, there is probably a calcium-concentrating system, so far undefined.

The more exact definition of the nucleating system remains a fascinating subject for further study. Some unanswered questions are outlined: (1) What is the chemical potential of nuclei formation? (2) What groups in the nucleating matrix participate in the capture of calcium and phosphate ions? (3) What is the role of mucopolysaccharides or mucoproteins? (4) How do energizing agents participate in nucleation? (5) What is the degree of specificity and selectivity of the nucleating mechanism? (6) What are the circumstances that bring about nucleation at abnormal sites in the body?

Crystal Growth

The growth of nuclei into ionic crystals depends on the maintenance of a state of supersaturation (metastable liquid phase) with respect to the nuclei. Another factor, according to Turkevitch, is the presence of an impurity.[27] The "driving force" for further growth requires physical or chemical imperfections. This is in harmony with Frank's concept of spiral dislocation, a self-perpetuating surface imperfection, which permits the addition of ions layer by layer.[28]

Regarding the rate of growth of bone hydroxyapatite crystals, which are of colloidal dimensions, it is interesting to consider the law of growth of fine particles:[27] the rate of growth of a colloidal particle is proportional to its diameter (the larger the particle the faster it grows; the smaller the particle the slower it grows). This also follows from equations for the solubility product of calcium phosphate, in which the rate of growth

decreases as the surface-to-volume ratio approaches zero.[7] This is in contrast to the rate of growth of larger crystals, where the rate is inversely proportional to the diameter.[29] The initial aggregate, probably a more soluble calcium phosphate such as $CaHPO_4$, undergoes transformation to $Ca_{10}(PO_4)_6(OH)_2$, which is less soluble than $CaHPO_4$ and is likely to grow more rapidly. The increased velocity of crystal growth after transformation and with increasing diameter may explain why osteons are already at least 70 per cent mineralized by the time they are discernible and may account, too, for the extremely rapid rate of calcification.[8]

Habit modification. The character of the final bone crystal depends on the basic lattice structure, as well as the influence of trace impurities in modifying the shape of the growing crystal. The action of such impurities, referred to as habit modifiers, is illustrated in FIGURE 4.[30] Habit modification occurs in hydroxyapatite on exposure to various concentrations of citrate, which affect both size and shape of the crystals.[31] Dyes that can be preferentially adsorbed on one facet of a crystal can modify

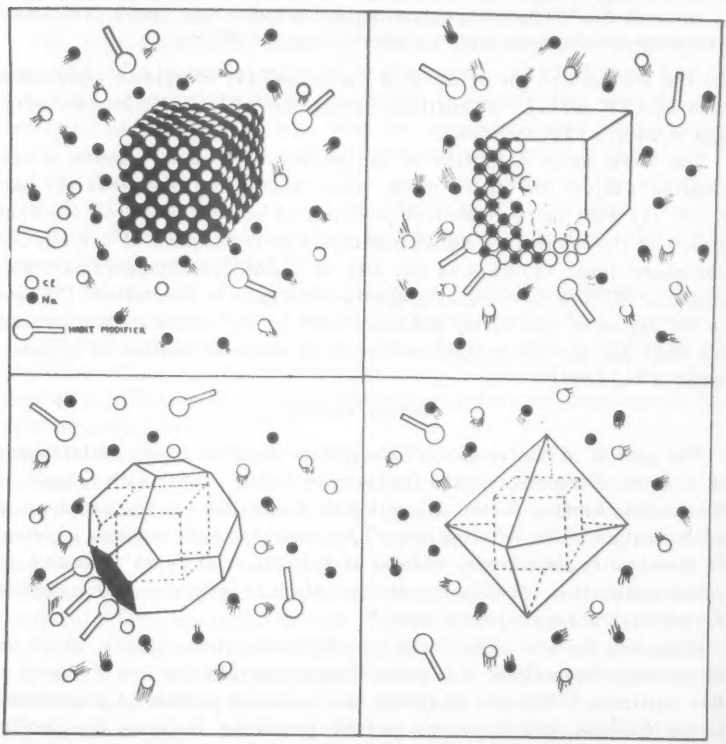

FIGURE 4. Stages in the modification of habit of sodium chloride crystal from cubic to octahedral.

its growth so that it takes place more rapidly in other planes.[32] As a simple example, if growth of the crystal is uninhibited, all facets grow at their normal rate (FIGURE 5a and b). If two of three dimensions are inhibited from further growth, then the inhibited plane will remain small and the third dimension will elongate. The growing crystal, confined as in a "straitjacket," will enlarge in the long axis (FIGURE 5a and c). Inhibiting forces applied continuously can cause convergence of the elongating crystal to a point, that is, dimensions of facets in the inhibited plane will gradually decrease to zero. Crystal growth will then cease (FIGURE 5a and *d*).

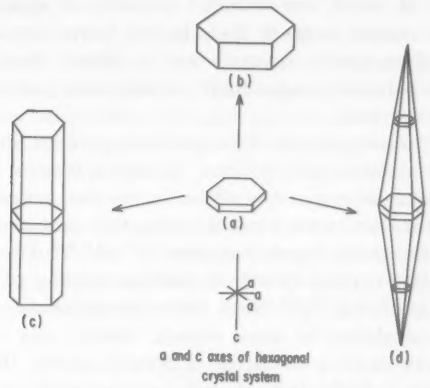

FIGURE 5. Habit modification of hexagonal crystal *(schematic): (a)* original hexagonal crystal; *(b)* hexagonal crystal after further growth with no habit modification; *(c)* habit modification with convergence of *a*-axes to a point, while the crystal elongates in its c-axis. Such habit modification would result from surface inhibition of the initially rectangular planes, which continues to be applied, while additional material is being deposited on the hexagonal ends. Here the hexagonal dimensions decrease with continued inhibition until a point (or zero dimensions) is reached and crystal growth stops.

In bones and teeth habit modifiers (or conceivably mechanical barriers) appear to be arranged favorably for the longitudinal growth of crystals in the direction of greatest mechanical strength. The orientation of apatite crystals[2-4] parallel with respect to collagen fibers in bone carries the implication that collagen or some group or compound bound to collagen (for example, mucoprotein or mucopolysaccharide) may be a habit modifier. The habit of the crystals may be attributable to their attachment to some portion of the fibrous macromolecule, so that longitudinal growth is much more rapid than transverse growth. It is difficult to conceive of modifiers other than some portion of the collagen that would orient the crystals parallel to the collagen fibril.

Estimated size of bone crystals. The largest hydroxyapatite crystal that has been prepared in the laboratory is 2.0 mm., or 2×10^7 Å.[33] In

bones and teeth the hydroxyapatite crystals are much smaller. Carlström *et al.* report a crystal 640 Å long,[34] and previously reported a smaller crystal 220 Å in length.[2] Enamel crystals as long as 1,600 to 6,000 Å have been observed.[3,6,35] The possibility has been proposed, however, that the larger enamel crystal is composed of smaller units of 300 Å held together by organic fibers.[36] Recent observations of Molnar[37] lend strength to the suggestion of Fabry[38] that the ultimate bone crystal is a fused aggregate of microcrystals rather than the product of extended growth of single crystals. Electron microscope studies of parietal bone in very young mice reveal crystals traced to lengths of as much as 3000 to 4000 Å, all of which demonstrated subunits of approximately 50 Å length.[37] Such results suggest that, in the body, factors limiting the size of the hydroxyapatite crystals are in effect when they are still well within the colloidal range. Habit modification probably contributes to the small crystal size.

Cessation of crystal growth. Two general concepts of the mechanism of cessation of crystal growth have become subjects of speculation:

(1) Certain ions or compounds adsorbed on the surface of a crystal in bonds stronger than those exerted among the ions composing the lattice may interfere with crystal growth.[32,33,40,41] The reversible inhibition of apatite crystal growth by surface binding of beryllium ions has been demonstrated.[40,41] Such ions as carbonate and citrate, or possibly polyphosphates or some organic cation, may be proposed as surface inhibitors causing cessation of crystal growth. Our studies indicate that in the calcification of collagen, as well as in preosseous cartilage, crystals are attached to the organic matrix.[14] Thus groups in the matrix, coming into firmer contact with the larger crystals, may be the equivalent of a surface inhibitor. Preferential attachment to certain surfaces is offered as an explanation of inhibitors of crystal growth that become effective only when the crystals reach a certain size, in contrast to inhibitors that are attached to all surfaces and stop growth at a wide range of sizes.

(2) A second concept of the cessation of crystal growth is based on the assumption of decreased contact with extracellular fluid as the crystal matures; thus the components for crystal growth are not available. Both mechanisms may be visualized as playing a role in the cessation of crystal growth, since the mature crystal is in contact with the collagen fiber without any appreciable water space.

Composition of bones and teeth. The composition of calcified tissues *in vivo* is related to the composition of blood serum, which can be regulated by the diet.[5,42] The amount of carbonate adsorbed depends on the CO_3:PO_4 ratio of the solution,[5,42,43] which is a function of the ratio of $[Ca^{++}][CO_3^{=}]$ to $[Ca^{++}][HPO_4^{=}]$. Similarly, it is likely that strontium deposition is related to the ratio of $[Sr^{++}][HPO_4^{=}]$ to $[Ca^{++}][HPO_4^{=}]$, and thus to the Sr:Ca ratio.

Summary

Nucleation in mineralizing tissues requires a solution phase whose chemical potential $[A_{Ca}{}^{++}][A_{HPO_4}{}^{=}]$ is above that of the nuclei. The active nucleating center is visualized as a site or adjacent sites between collagen protofibrils capturing a cluster of calcium and phosphate ions. The shape of the active center is specific for conversion of the captured ions to a nucleus via a lock-and-key mechanism. The complete system probably contains a mucoprotein, the glycolytic cycle, ATP and UTP, and a postulated calcium-concentrating mechanism. Subsequent growth of apatite crystals proceeds at a lower chemical potential than that required for nuclei formation.

The rate of growth is proportional to the diameter of the particles which are colloidal in size. Trace components can modify crystal habit and may be factors in determining the shape as well as the size of bone mineral crystals. Orientation of bone crystals parallel to the collagen fibrils implies that the organic matrix acts as a habit modifier.

Cessation of crystal growth is probably caused by surface inhibitors, and possibly decreased renewal of fluids surrounding the crystals. The inorganic composition of bone is related to the composition of the surrounding fluid. Variations in composition are visualized as occurring in the amorphous adsorption layer surrounding the crystal proper, while the crystalline core is visualized as hydroxyapatite of relatively constant composition.

References

1. McLEAN, F. C. & A. M. BUDY. 1959. Connective and supporting tissues: bone. Ann. Rev. Physiol. 21: 69.
2. CARLSTRÖM, D. & J. B. FINEAN. 1954. X-ray diffraction studies on the ultrastructure of bone. Biochim. et Biophys. Acta. 13: 183.
3. ROBINSON, R. A. 1951. Electron micrography of bone. Trans. Macy Conf. on Metabolic Interrelations. 3:271.
4. SCOTT, D. B. & F. F. LASIE. 1958. Electron microscopic study of anorganic enamel. Abst. #49. J. Dental Research. 37: 23.
5. SOBEL, A. E. 1955. Local factors in the mechanism of calcification. Ann. N.Y. Acad. Sci. 60(5): 713.
6. GINELL, R. 1955. A general theory of association. Ann. N.Y. Acad. Sci. 60(5): 521.
7. BEST, J. B. 1959. Some theoretical considerations concerning crystals with relevance to the physical properties of bone. Biochim. et Biophys. Acta. 32: 194.
8. NEUMAN, W. F. & M. NEUMAN. 1958. The Chemical Dynamics of Bone Mineral. Univ. Chicago Press. Chicago, Ill.
9. ROBISON, R. 1932. The Significance of Phosphoric Esters in Metabolism. New York Univ. Press. New York, N.Y.
10. ROBISON, R. & A. H. ROSENHEIM. 1934. Calcification of hypertrophic cartilage *in vitro*. Biochem. J. 28: 694.
11. GUTMAN, A. B. & T. F. YU. 1950. A concept of the role of enzymes in endochondral calcification. Trans. Macy Conf. on Metabolic Interrelations. 2: 167.

12. GUTMAN, A. B. & T. F. YU. 1951. A further consideration of the effects of beryllium salts on *in vitro* calcification of cartilage. Trans. Macy Conf. on Metabolic Interrelations. 3:90.
13. ALBAUM, H. G., A. HIRSCHFELD & A. E. SOBEL. 1952. Calcification. VI. Adenosine triphosphate content of preosseous cartilage. Proc. Soc. Exptl. Biol. Med. 79:238.
14. BACHRA, B. N. & A. E. SOBEL. 1959. Calcification. XXV. Mineralization of reconstituted collagen. Arch. Biochem. Biophys. 85:9.
15. BACHRA, B. N., A. E. SOBEL & J. W. STANFORD. 1958. The mineralization of collagen. Abst. IVth Intern. Congr. Biochem., Sect. 12(76). Vienna, Austria.
16. BACHRA, B. N., A. E. SOBEL & J. W. STANFORD. 1959. Calcification. XXIV. Mineralization of collagen and other fibers. Arch. Biochem. Biophys. 84:79.
17. SOBEL, A. E., M. BURGER & S. NOBEL. 1958. Calcification. XXI. Detection of nuclei of crystallization in rachitic cartilage. Proc. Soc. Exptl. Biol. Med. 99:341.
18. LAVINE, L. S., M. BURGER & A. E. SOBEL. 1957. The effect of bone bank preservation on the calcifying mechanism. J. Bone & Joint Surg. 39b:758.
19. SOBEL, A. E. & M. BURGER. 1954. Calcification. XIV. Investigation of the role of chondroitin sulfate in the calcifying mechanism. Proc. Soc. Exptl. Biol. Med. 87:7.
20. SOBEL, A. E. & A. HANOK. 1952. Calcification. VII. Reversible inactivation of calcification *in vitro* and related studies. J. Biol. Chem. 108:395.
21. SOBEL, A. E., P. A. LAURENCE & S. NOBEL. 1959. Mechanisms of nuclei formation in mineralizing tissues. Clin. Orthopaedica. In press.
22. SOBEL, A. E. & S. NOBEL. 1959. Nuclei formation and strontium deposition in rachitic bone. Am. Chem. Soc. 136th National Mtg., Div. Biol. Chem. Atlantic City, N.J.
23. BACHRA, B. N. & A. E. SOBEL. 1959. Calcification. XXVII. Collagen transformation under the influence of calcium and phosphate ions. Proc. Soc. Exptl. Biol. Med. 102:314.
24. GOLDENBERG, H. & A. E. SOBEL. 1954. Calcification. XII. Cation-linked inhibition by fluoride and cyanide ions in β-glycerophosphate medium. Proc. Soc. Exptl. Biol. Med. 85:275.
25. GOLDENBERG, H. & A. E. SOBEL. 1951. Calcification. V. Influence of fluoride and cyanide ions in the presence and absence of magnesium. Proc. Soc. Exptl. Biol. Med. 78:719.
26. SOBEL, A. E., H. GOLDENBERG & A. HANOK. 1951. Calcification. IV. Influence of strontium and magnesium ions on calcification *in vitro*. Proc. Soc. Exptl. Biol. Med. 78:716.
27. TURKEVITCH, J. 1959. The world of fine particles. Am. Scientist. 47:97.
28. FRANK, F. C. 1949. Discussions of the Faraday Society. Crystal Growth. 5:48-54. Gurney & Jackson, Ltd. London, England.
29. TIPSON, R. S. 1950. *In* Technique of Organic Chemistry. III:384. A. Weissberger, Ed. Interscience. New York, N.Y.
30. MILONE, M. & G. CETINI. 1958. Changement de habitus des cristaux au moyen des tensioactifs. Exhibit at Palais de la Science de l'Exposition Universelle de Bruxelles.
31. PATTERSON, D. 1954. Effect of a citrate ion impurity on the size and shape of calcium phosphate crystals. Nature. 173:75.
32. BUCKLEY, H. E. 1951. Crystal Growth. Wiley. New York, N.Y.
33. KOLTHOFF, I. M. & C. ROSENBLUM. 1933. The adsorption of ponceau 4R (new coccine) and methylene blue by lead sulfate and the influence of

adsorbed Ponceau on the speed of kinetic exchange. J. Am. Chem. Soc. 55: 2664.

34. CARLSTRÖM, D. & J. E. GLAS. 1959. The size and shape of the apatite crystallites in bone as determined from line broadening measurements on oriented specimens. Biochim. et Biophys. Acta. 35:46.
35. FRANK, R. & R. F. SOGNNAES. 1958. Symposium on calcification in biological systems. Dental aspects of mineralization with special reference in the ultrastructural pattern of enamel. Am. Assoc. Advancement Sci. Meeting. Washington, D.C.
36. SCOTT, D. B. & F. F. LASIE. 1958. Electron microscopic study of anorganic enamel. Abst. #49. J. Dental Research. 37: 23.
37. MOLNAR, Z. 1960. Additional observations on bone crystal dimensions. Clin. Orthopaedica. In press.
38. FABRY, C. 1958. La structure des phosphates de calcium apatitiques. Bull. Soc. Chim. Biol. XL: 1333.
39. HAYEK, E., W. BOHLER, J. LECHLEITNER & H. PETTER. 1958. Hydrothermal synthesis of calcium apatites. Z. anorg. u. allgem. Chem. 295:241.
40. SOBEL, A. E., J. SAMACHSON & S. NOBEL. 1958. Calcification. XVII. Inhibition of nuclei formation and growth. Arch. Biochem. Biophys. 77:89.
41. SAMACHSON, J., S. NOBEL & A. E. SOBEL. 1959. Calcification. XXII. A method of studying crystal growth. J. Dental Research. 38: 253.
42. SOBEL, A. E. 1955. Composition of bones and teeth in relation to blood and diet. Overdruk uit "Voeding." 16: 567.
43. NEUMAN, W. F. & M. W. NEUMAN. 1953. The nature of the mineral phase of bone. Chem. Rev. 53: 1.

ACTION OF LUNG CHEMORECEPTORS ON THE CARDIOINHIBITORY CENTER*

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The effectiveness of the circulatory system depends on its adjustments to bodily requirements. These adjustments can be of intrinsic or extrinsic nature: they can depend on the inherent properties of the cardiac and vascular tissues, or on external influences such as those exerted by the autonomic nervous system.

It is the purpose of this paper to review some observations concerning the extrinsic factors that control heart rate.

The heart rate is determined by cardioaccelerator and cardioinhibitor reflexes. The relative magnitude of these influences depends largely on the afferent circulatory information.

The circulatory system contains receptors that are sensitive to blood pressure, cardiac frequency and blood oxygen saturation. The discharges of these receptors will activate compensatory reflexes, that is, reflexes that tend to produce variations in the direction opposite to the changes that activate them (negative feedback). The result will be a more accurate adjustment of the heart rate to different requirements.

Anatomical Remarks

This afferent information is first integrated in the corresponding medullary centers. We shall consider as "cardioinhibitory center" that part of a cardioinhibitory reflex located in the medulla without regard to its precise anatomical location (FIGURE 1).

The receptors connected to this center are numerous, but, in so far as is known, most of their afferent messages arrive through the vagi and glossopharyngeal nerves. These receptors are sensitive to blood pressure changes (as are those located in the aortic arch and carotid sinus) and to other factors, such as pulmonary or visceral stretch. There are also receptors sensitive to blood oxygen saturation changes (such as those located in the aortic and carotid glomi), but there is disagreement as to whether they activate also the cardioinhibitory center (for detailed discussion see Alvarez-Buylla, 1951; Heymans and Neil, 1958; and Korner, 1959).

*This paper, illustrated with slides, was the first of two papers presented at a meeting of the Section on January 11, 1960.

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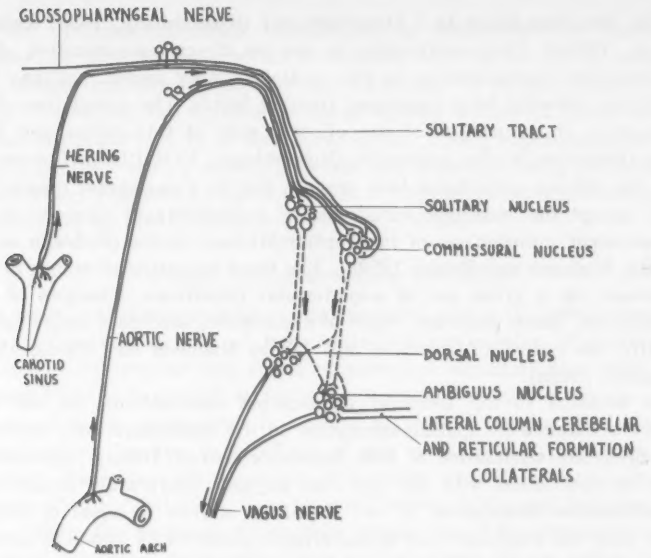

FIGURE 1. Diagram of the central pathways of the cardioinhibitory reflexes described in this paper. Afferent fibers (the aortic nerve and Hering's nerve) make their first synaptic relay at the nucleus solitarius and commisural nucleus. Vagal fibers, originating in the dorsal nucleus, constitute the efferent pathway. There is no direct histological evidence for the possibility that a great number of fibers extends from the sensory to the motor nuclei (Cajal, 1909); their existence is therefore inferred from physiological evidence *(broken lines)*. The view commonly held is that efferent cardiac vagal branches originate from the dorsal nucleus. However, no critical study is known to the author that rules out contributions from the ambiguous nucleus. Arrows indicate pathways normally active during physiological or electric stimulation of the afferent nerves.

In the rabbit the baroreceptors of the aortic arch are separated from the rest of the vagus constituting the depressor or Cyon-Ludwig nerve. Stimulation of the central end of this nerve produces diminution of the heart rate. This effect is due chiefly to an increase of vagal activity, although there is also a delayed decrease of the sympathetic tone without significance for short periods of stimulation (Bronk *et al.*, 1936; Alexander, 1946).

Input-Output Relationships During Normal Ventilation

The correlation between the stimulus (input) and the magnitude of the decrease of heart rate (output) gives us an idea of the degree of reflex excitability of the cardioinhibitory center. Bradycardia obtained by stimulation of the central end of the depressor nerve increases as frequency or intensity of stimulation is increased. In the lightly anesthetized

rabbit this correlation is a hyperbolic one (Rosenblueth, 1934; Rudomin *et al.*, 1959*a*). This relationship is not the direct representation of the input-output characteristics of the cardioinhibitory center, because it is partially distorted by a peripheral limiting factor. The correlation of the frequency of stimulation of the efferent side of this reflex and heart rate diminution is also hyperbolic (Rosenblueth, 1934,1950). However, as all the effects considered here are not due to a peripheral change, we can accept the observed variations as indications of changes in the input-output correlations of the cardioinhibitory center (Rudomin *et al.*, 1959*a*; Rudomin and Rubio, 1959*b*). The input-output relationship is very constant for a given set of experimental conditions. Changes of lung ventilation, blood pressure, depth of anesthesia, and blood sugar content modify the output (Rudomin *et al.*, 1959*a*; Rudomin and Rubio, 1959*b*; Rudomin 1960*a*).

In addition to the temporal input-output correlations, we can also study occurence of spatial summation in the cardioinhibitory center by simultaneous stimulation of both depressor nerves. During hyperventilation or ventilation with 100 per cent oxygen, bradycardia produced by simultaneous stimulation of both depressor nerves is equal or slightly less than the algebraic sum of the effects produced by separate stimulation of either nerve. This reveals a small degree of central occlusion (Creed *et al.*, 1932). During normal ventilation small degrees of occlusion or of facilitation are usually found (Rudomin *et al.*, 1959*a*).

The relative distributions of the vagal output between the two vagi nerves depend upon the pulmonary ventilation. During hyperventilation or ventilation with 100 per cent oxygen bradycardia obtained by stimulation of the depressor nerve is due chiefly to activation of the ipsilateral vagal efferent pathways. Thus there is a limited central crossing (Heymans, 1929; Reed and Scott, 1955; Rudomin *et al.*, 1959*a*). During normal ventilation central crossing is slightly increased.

Input-Output Correlations During Hypoxia and Hypoventilation

During moderate hypoxia or hypoventilation, reflex responses obtained by stimulation of the depressor nerve are increased (Van der Linden, 1933; Verlot, 1935; Schmidt and Comroe, 1940; Rudomin *et al.*, 1959*a*); that is, the hyperbolic curve that correlates input-output is shifted above the one obtained during hyperventilation or normal ventilation. This suggests that the reactivity of the system is increased (Cannon and Rosenblueth, 1949). In a similar way, the small degree of occlusion seen during hyperventilation is transformed into facilitation. Central crossing is also increased, showing that the contralateral vagal efferent contribution is enhanced (Tournade and Malmejac, 1931; Wang and Borison, 1947; Rudomin *et al.*, 1959*a*).

This increase of reflex excitability is independent of pulmonary volume, because the same effect is obtained when the animal is breathing low oxygen gaseous mixtures without changing the stroke volume of the pump. Therefore, the facilitation obtained may be due to direct central action of oxygen lack or to the excess of CO_2 during hypoventilation, and to oxygen lack during anoxia (Schmidt and Comroe, 1940), or to an indirect effect produced by the activation of the circulatory chemoreceptors (Gellhorn *et al.*, 1942; Rudomin and Rubio, 1959*b*).

Effects of Chemoreceptor Activation

In order to obtain more information about the role of the chemoreceptors upon reflex excitability of the cardioinhibitory center, Rudomin and Rubio (1959*b*) studied the effect of selective stimulation of these receptors by injecting small amounts of potassium- or sodium-cyanide. The action of these substances is similar to that of oxygen lack, and is considered to be due to blockage of the respiratory cytochromes (for detailed discussion of the action of cyanide upon chemoreceptors see Alvarez-Buylla, 1951,1954; Schmidt and Comroe, 1940; and Heymans and Neil, 1958). The response obtained by stimulation of the depressor nerve is much increased when stimulation is done 5 to 10 sec. after intravenous injection of 50 μg. of KCN. Spatial and temporal summation, as well as central crossing, are also increased. This facilitatory effect depends on the amount of cyanide injected. However, this drug produces only slight, or no, bradycardia when injected in the same amounts without depressor nerve stimulation (FIGURE 2).

Site of Origin of the Facilitatory Action of Cyanide

The facilitatory action obtained by cyanide injection is greater when the injection is made into the jugular vein, right auricle, or pulmonary artery than when the same amounts are injected into the brachiocephalic trunk or left auricle. This suggests that facilitation is due to activation of receptors located in the venous side of the circulation, possibly the lung. It also excludes the possibility that the facilitatory effect of cyanide is due to direct activation of the cardioinhibitory center (FIGURE 3).

The hypothesis that the receptors stimulated are in the lungs was tested in subsequent experiments. Injection of cyanide into the circulation of an isolated lung, perfused by a donor rabbit, also facilitates the cardioinhibitory reflex (Rudomin and Rubio, 1959*b*). Once again, the injection of the same amount of cyanide, without subsequent stimulation of the depressor nerve, fails to produce any observable effect. Furthermore, it has also been found that cyanide facilitation can be elicited by putting small areas of filter paper soaked in cyanide solution upon the lung. This effect varies with the surface exposed to cyanide, and

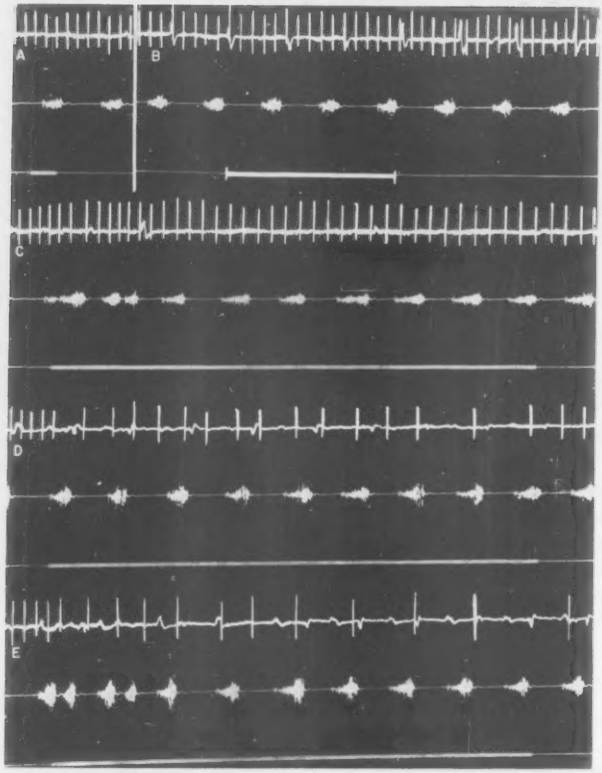

FIGURE 2. Rabbit anesthetized with Nembutal (20 to 25 mg./kg.) Precordial derivations for recording heart rate *(upper record)* and diaphragmatic electromyogram *(lower record)*. *(A)* Control values before I.V. injection of 100 μg. of KCN. Black bar below signals the time of injection. *(B)* Record taken 5 sec. after *A*. The only noticeable effect is an increase in the respiratory activity without changes in cardiac frequency. *(C)* Effect of stimulation of the central ends of both depressor nerves with supramaximal shocks delivered at 16/sec. *(D)* Same as *C*, but 15 sec. after I.V. injection of 100 μg. of KCN. *(E)* Same as *C*, but after I.V. injection of 200 μg. of cyanide. Long bars signal stimulation of the depressor nerves. Time calibration in record *B*, 5 sec. Reproduced from Rudomin and Rubio, 1959*b* by permission of *Acta Physiologica Latinoamericana*. Records retouched.

does not disappear when the corresponding pulmonary veins and arteries are temporarily occluded. No facilitatory action is observed when the filter paper is put in contact with other thoracic structures.

The facilitatory action of cyanide was also obtained after thoracic sympathectomy and/or high spinal cervical section (C_5-C_6). Bilateral vagotomy or atropinization abolished this facilitatory action. It may be

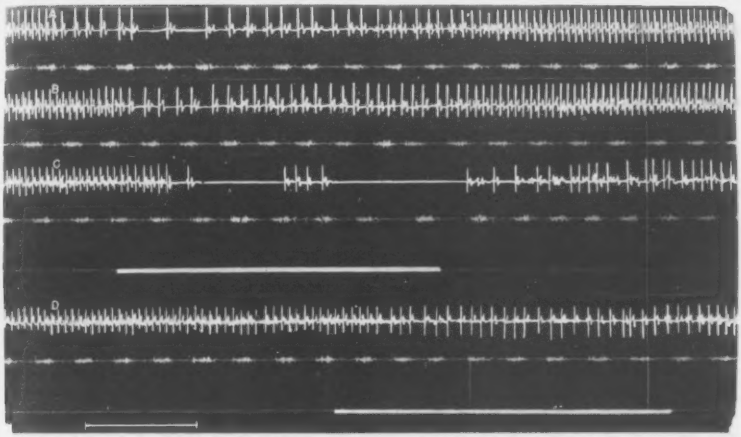

FIGURE 3. Effects obtained by supramaximal stimulation of the central end of both depressor nerves (32/sec.) after 50 μg. potassium cyanide injections. All injections were applied at the beginning of the records. *(A)* Left auricle injection. *(B)* Brachiocephalic trunk injection. *(C* and *D)* Right auricle injections. Black bar below *C* signals time of stimulation of the depressor nerves for *A*, *B*, and *C*. Black bar below *D* signals stimulation for *D*. *Upper records*, heart rate; *lower records*, diaphragmatic activity. Time calibration, 5 sec. Control effects of depressor nerve stimulation were similar to those shown in *D*. For further explanation see text. Reproduced from Rudomin and Rubio, 1959*b* by permission of *Acta Physiologica Latinoamericana*. Records retouched.

concluded that injection of cyanide activates pulmonar vagal afferent structures. The signals of these receptors, although producing no measurable change themselves, enhance the reflex excitability of the cardioinhibitory center. This subliminal effect has a short latency (2 to 3 sec.) and lasts only 5 to 10 sec. after the intravenous injection. This finding explains perhaps why several investigators have failed to find any reflex effects by changing the oxygen and CO_2 concentration or injecting cyanide in the circulation of a perfused lung (Aviado *et al.*, 1951; Dawes and Comroe, 1954).

Influence of the Stimulation of the Brain Stem Reticular Formation

In a further study (Rudomin, 1960*b*), an attempt was made to determine the central mechanism of the facilitation produced by cyanide injections. It was found that the activation of the medial bulbar reticular formation (depressor area in the floor of the IV ventricle) facilitates cardioinhibitory reflexes. In contrast, stimulation of the lateral bulbar reticular formation abolishes them. The mechanism of this inhibitory effect is perhaps similar to that obtained by stimulation of the lateral bulbar reticular formation upon afferent transmission in the first synaptic relays

of the dorsal column nuclei (Hernández-Peón and Scherrer, 1955; Scherrer and Hernández-Peón, 1955). Any attempt to explain the facilitatory action of cyanide-sensitive lung receptors must take into account the existence of facilitatory and inhibitory bulbar areas. Further experiments are needed to determine whether the afferent fibers are related to one or more of these areas.

Possible Physiological Role of the Lung Chemoreceptors

During anoxia the carotid body chemoreceptors are activated intensely (Heymans and Neil, 1958). It is possible that lung receptors sensitive to cyanide are also stimulated during anoxia and hypoventilation and that this effect contributes in part to the enhancement of reflex excitability of the cardioinhibitory center. If this is the case, reflex integration of the circulatory system becomes complicated by the possibility of reflex control of the effectiveness of the circulatory homeostatic reflexes. Lung chemoreceptors may then determine the degree of negative feedback in those reflexes. However, there is need for further experimental evidence to show whether these receptors are stimulated during anoxia and whether they produce tonic discharges during normal ventilation.

Summary

Reflex excitability of the cardioinhibitory center is greatly increased during hypoxia, hypoventilation, and intravenous injections of sodium cyanide or potassium cyanide.

Evidence is presented to show that the facilitatory effect of cyanide injections is due to stimulation of pulmonary vagal receptors. Activity of these receptors, even though producing no measurable changes themselves, enhances reflex excitability of the cardioinhibitory center.

Acknowledgment

I am indebted to V. B. Brooks for his valuable assistance in the translation of the manuscript.

References

ALEXANDER, R. S. 1946. Tonic and reflex functions of medullary sympathetic centers. J. Neurophysiol. 9: 205.

ALVAREZ-BUYLLA, R. 1949. Analisis experimental de la función del nervio depresor aortico. Mem. Rev. Acad. Nac. Cienc. Mexico. 56: 383.

ALVAREZ-BUYLLA, R. 1951. Actividad quimiorreceptora del seno carotídeo. Arch. Inst. Cardiol. Mexico. 21: 408.

ALVAREZ-BUYLLA, R. 1954. Disociación de las actividades quimiorreceptoras y barorreceptoras en gatos. Arch. Inst. Cardiol. Mexico. 24: 26.

AVIADO, D. M., T. U. LI, W. KALOW, C. F. SCHMIDT, G. L. TURBULL, G. W. PESKIN, M. E. HESS, & A. J. WEISS. 1951. Respiratory and circulatory reflexes from the perfused heart and pulmonary circulation of the dog. Am. J. Physiol. 165: 261.

BRONK, D. W., L. K. FERGUSON, R. MARGARIA & D. Y. SOLANDT. 1936. The activity of the cardiac sympathetic centers. Am. J. Physiol. 117: 237.

CANNON, W. B. & A. ROSENBLUETH. 1949. The Supersensitivity of Denervated Structures. A Law of Denervation. Harper. New York, N.Y.

COMROE, J. H., JR. 1939. The location and function of the chemoreceptors of the aorta. Am. J. Physiol. 127: 176.

CREED, R. S., DENNY-BROWN, J. C. ECCLES, E. G. T. LIDELL & G. S. SHERINGTON. 1932. Reflex Activity of the Spinal Cord. Oxford Univ. Press. :31. London, England.

DAWES, S. G. & J. H. COMROE. 1954. Chemoreflexes from the heart and lungs. Physiol. Rev. 34: 167.

GELLHORN, E., R. CORTELL & H. B. CARLSON. 1942. Fundamental differences in excitability of somatic and autonomic centers in response to anoxia. Am. J. Physiol. 135: 641.

HERNÁNDEZ-PEÓN, R. & H. SCHERRER. 1955. Inhibitory influence of brain stem reticular formation upon synaptic transmission in trigeminal nucleus. Federation Proc. 14: 71.

HEYMANS, C. 1929. Le sinus Carotidien, zone réflexogène régulatrice du tonus vagal cardiaque du tonus neurovasculaire et de l'adrénalinosecrétion. Arch. Intern. Pharmacodynamie. 35: 269.

HEYMANS, C. & E. NEIL. 1958. Reflexogenic areas from the cardiovascular system. Churchill. London, England.

KORNER, P. I. 1959. Circulatory adaptations in hypoxia. Physiol. Rev. 39: 687.

RAMÓN Y CAJAL, S., 1909. Histologie du système nerveux. Chap. XXVI. Reprinted by Consejo Superior de Investigaciònes Cientificas, Instituto Ramòn y Cajal, 1952. Madrid, Spain.

REED, E. A. & J. C. SCOTT. 1955. Factors influencing the carotid sinus cardio-inhibitory reflex. Am. J. Physiol. 181: 21.

ROSENBLUETH, A. 1934. Central excitation and inhibition in reflex changes of heart rate. Am. J. Physiol. 107: 293.

ROSENBLUETH, A. 1950. The Transmission of Nerve Impulses at Neuroeffector Junctions and Peripheral Synapses. Mass. Inst. Technology Press. Cambridge, Mass.

RUDOMIN, P., D. ERLIJ & P. EBERSTADT. 1959*a*. Influence of hypoxia and hypoventilation upon spatial and temporal summation of the cardio-inhibitory center. Acta Physiol. Latinoam. 9: 203.

RUDOMIN, P. & R. RUBIO. 1959*b*. Subthreshold activity of potassium cyanide chemoreflexes. Acta Physiol. Latinoam. 9: 194.

RUDOMIN, P. 1960*a*. Influence of asphyxia, anesthesia and some drugs upon the reflex excitability of the cardio-inhibitory center. Acta Neurol. Latinoam. In press.

RUDOMIN, P. 1960*b*. Influence of brain stem reticular formation upon reflex activation of the cardio-inhibitory center. Acta Neurol. Latinoamer. In press.

SCHERRER, H. & R. HERNANDEZ-PEÓN. 1955. Inhibitory influence of reticular formation upon synaptic transmission in gracilis nucleus. Federation Proc. 14: 132.

SCHMIDT, C. F. & J. H. COMROE. 1940. Functions of carotid and aortic bodies. Physiol. Rev. 20: 115.

TOURNADE, A. & J. MALMEJAC. 1931. Nerves vaso-sensibles et adrenalino-secretion. Compt. rend. soc. biol. 106: 444.

VAN DER LINDEN, P. 1933. Influences de l'acapnie, de l'anoxemie, du CO_2, de l'eserine, de la prostigmine et du numal sur les réflexes cardio-inhibiteurs du sinus carotidien. Arch. Interm. Pharmacodynamie. 46: 63.

VERLOT, M. 1935. Influences de l'adrenaline et de l'essérine sur le système cardio-inhibiteur vagal. Compt. rend soc. biol. 118: 1485.

WANG, S. C. & H. L. BORISON. 1947. Decussation of pathways in carotid sinus cardio-vascular reflexes: example of principle of convergence. Am. J. Physiol. 150: 722.

EFFECT OF PENTOBARBITAL AND MEPERIDINE ON THE CENTRAL RESPIRATORY MECHANISMS IN THE CAT*

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A previous report[1] has proposed that normal respiratory rhythm originates in the pontile apneustic center with periodic modulation by the inhibitory impulses from the pneumotaxic center in the rostral pons and the pulmonary vagal afferent nerves. Pontile transection and bilateral vagotomy resulted in apneusis (prolonged inspiratory spasm) or apneustic breathing, which changed to "gasping" respiration by transection to remove the pons. A further study has suggested that the pneumotaxic center serves to facilitate the phasic activity of the lower respiratory centers.[2] In animals with intact vagus nerves destruction of the pneumotaxic center caused slowing of respiration. Electric stimulation of the pneumotaxic center elicited respiratory acceleration with inspiratory shift,[2,3] a response similar to that obtained during low-frequency central vagal stimulation.[4]

Pentobarbital can reduce both the rate and depth of respiration. Harris and Borison,[5] working on the cat, have shown that respiratory rhythmicity is particularly susceptible to the action of this agent. Spontaneous breathing first became slow and subsequently failed long before the inspiratory center became inexcitable to electric stimulation. Furthermore, the evoked inspiratory response was progressively decreased in magnitude with cumulative doses of pentobarbital. The duration of inspiration was prolonged after thiopental.[6] These observations suggest that, in addition to their depressant effect on the medullary respiratory centers, barbiturates have a predominantly depressant action on the pontile respiratory mechanisms concerned with the modulation and facilitation of phasic respiratory activity. The present study examined this action of pentobarbital by comparing the respiratory responses elicited by electric stimulation of the pontile pneumotaxic center, the medullary inspiratory center, and the central vagus nerves before and after intravenous administration of cumulative doses of pentobarbital to decerebrate cats.

Meperidine also reduces the rate and depth of respiration.[7,8] With higher doses it produces irregular rhythm and, ultimately, apnea. However, the experiments previously reported were carried out on anesthetized animals in which the presence of anesthetic agent could either potentiate

* This paper, illustrated with slides, was the second of two papers presented at a meeting of the Section on January 11, 1960. The work described in this article was supported by Research Grant B31C from the National Institute of Blindness and Neurological Diseases, Public Health Service, Bethesda, Md. A preliminary report of this work was presented before the XXI International Congress of Physiological Sciences, Abstract: 199, on August 10-15, 1959, in Buenos Aires, Argentina.

or modify the respiratory depressant effect of the drug under consideration. Since the effect of meperidine on various functional components of the central respiratory mechanisms has not been investigated, a study of this problem in unanesthetized, decerebrate cats was undertaken.

Midcollicular decerebration was performed on the cat under diethylether anesthesia. The animal was then allowed to breath room air for at least one hour so that most of the ether was exhaled. A bilateral vagotomy was done. Respiratory movements were then recorded with a small animal spirometer connected via a soda lime absorber to the trachea. A small amount of oxygen was continuously fed into the spirometer to keep the tracings leveled.

With the aid of a stereotaxic instrument, enameled coaxial electrodes were inserted into the brain stem for the stimulation of the pneumotaxic

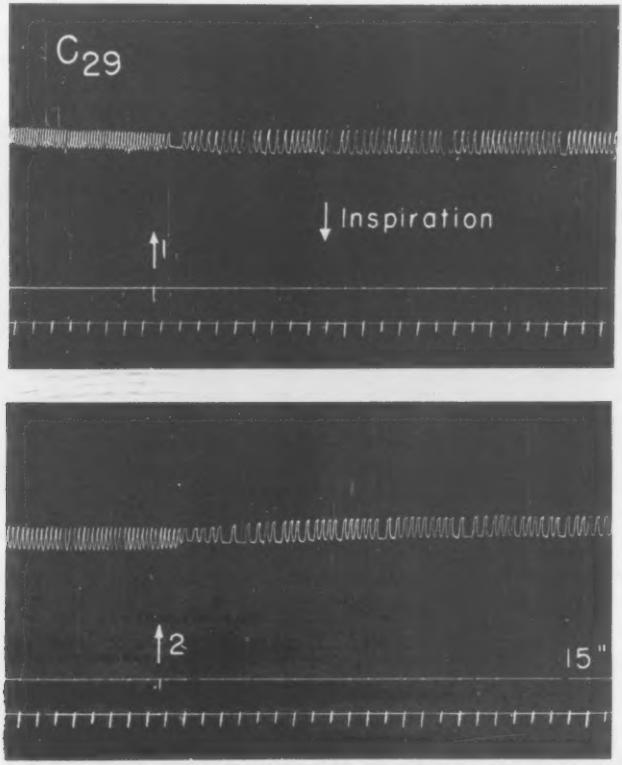

FIGURE 1. Cat 29, 2.6 kg. Midcollicular decerebrate, vagotomized. At arrow 1, 3 mg./kg., and arrow 2, 6 mg./kg. pentobarbital was given intravenously. Note prolonged inspiration after injections and reduced depth of respiration after second injection.

center and/or the medullary inspiratory center. Currents of rectangular pulses were derived from Grass stimulators (Model S4C) through their respective stimulus isolation units. The pontile pneumotaxic center and the medullary inspiratory center were identified by the characteristic respiratory responses elicited during electric stimulation as described in an earlier publication.[2] Stimulation of the pneumotaxic center caused respiratory acceleration with or without inspiratory shift. Stimulation of the inspiratory center produced a classic inspiratory spasm (FIGURE 2A). Stimulating currents of various intensities were used to establish the stimulus threshold as well as the magnitude of responses prior to drug injection. For central vagal stimulation a Palmer bipolar electrode was used. The stimulating currents were varied in intensity and frequency, the latter ranging from 10 to 200 shocks/sec. After a series of control stimulations, small increments of pentobarbital in doses of 3 to 6 mg./kg. or of meperidine in doses of 0.5 to 2.0 mg./kg. were injected intravenously at intervals of 10 to 20 min. After each dose the series of stimulations was repeated.

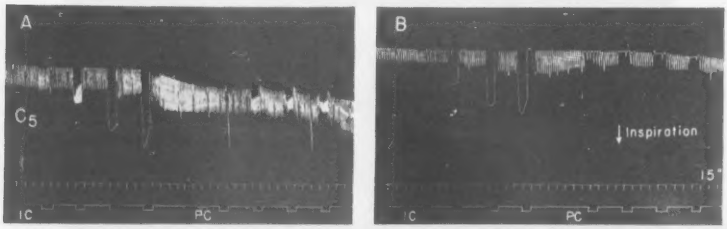

FIGURE 2. Cat 5, 2.7 kg. Midcollicular decerebrate, vagotomized. *Panel A:* control, IC, inspiratory center stimulation with currents of 50 shocks/sec.; pulse duration, 2 msec.; and voltage, 0.85, 1.5, 2, and 3 volts. PC, pneumotaxic center stimulation, frequency and duration, same as above; voltage, 1.5, 2, 3, and 4 volts. Between A and B, pentobarbital, 18 mg./kg., in 6 divided doses, was given intravenously. *Panel B:* IC, inspiratory center stimulation, voltage, 2, 3, 4, and 5 volts; PC, pneumotaxic center stimulation, voltage, 2, 3, 4, and 5 volts; frequency and duration, same as above.

For the first few minutes after the administration of pentobarbital there was a tendency toward the development of prolonged inspiration or of inspiratory pauses. After this period, respiration appeared normal and regular in rhythm (FIGURE 1). As the cumulative dose of pentobarbital increased, respiration became slow and shallow. When the total dose reached 24 to 30 mg./kg., the respiratory movements became extremely shallow with prolonged inspiratory and expiratory pauses, resembling those of apneustic breathing except for the depth.

The responses to stimulation of the pneumotaxic center and inspiratory center were essentially unaltered after small doses of pentobarbital (for controls, see FIGURE 2A). After each injection, the stimulus threshold

of the inspiratory center was progressively elevated, while the magnitude of the respiratory response was concurrently decreased. After a cumulative dose of pentobarbital of 18 to 24 mg./kg. had been attained (FIGURE 2B), respiratory acceleration and inspiratory shift could not be elicited upon stimulation of the pontile pneumotaxic center. Instead, there was expiratory apnea for the duration of stimulation. With threshold stimuli, the respiration was made slower and more shallow and was accompanied by expiratory pauses.

Central vagal stimulation with low-frequency currents (10 shocks/sec.) resulted in respiratory acceleration with an inspiratory shift. High-frequency stimulation (100 to 200 shocks/sec.) caused expiratory apnea. Pentobarbital did not alter these responses other than to reduce or eliminate the inspiratory shift during low-frequency stimulation. Even after relatively large doses of pentobarbital, when the respiration became extremely slow with prolonged inspiration it could still be accelerated by low-frequency stimulation.

In contrast to pentobarbital, meperidine decreased the respiratory rate and caused expiratory pauses. The "apneustic" tendency observed with pentobarbital was not evident. Immediately after an injection of meperidine, the depth of respiration was reduced and, after a few minutes, it was not significantly different from that of controls except for an occasional tendency toward irregularity both in the rate and depth (FIGURE 3).

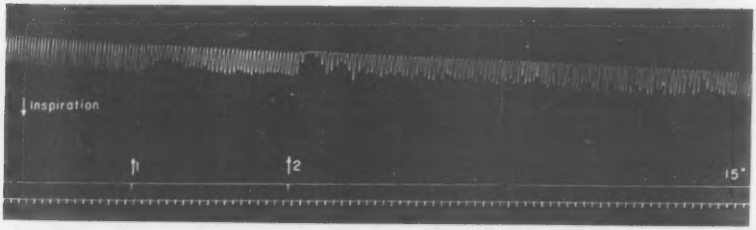

FIGURE 3. Cat 58, 4 kg. Midcollicular decerebrate, vagotomized. At each arrow, 2 mg./kg. of meperidine was given intravenously. Note transient apnea and decrease in respiratory amplitude, followed by slowing of respiration and irregularity after second injection.

After 2 to 3 mg./kg. of meperidine, the stimulus threshold of the inspiratory center was slightly elevated, but the magnitude of the inspiratory response remained essentially the same (FIGURE 4). The characteristic respiratory acceleration upon pneumotaxic center stimulation was abolished. Instead, there was an inspiratory standstill for the duration of the stimulation. The response to low-frequency central vagal stimulation was altered in a similar fashion. High-frequency vagal stimulation still produced expiratory apnea (FIGURE 5).

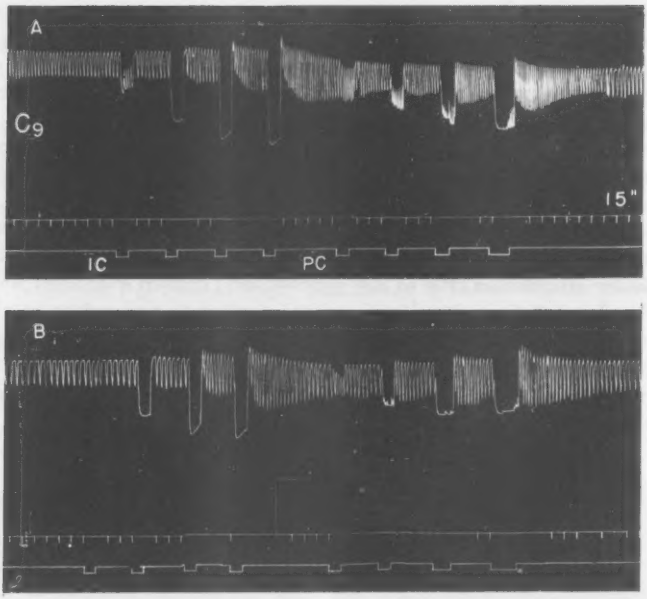

FIGURE 4. Cat 9, 2.3 kg. Midcollicular decerebrate, vagotomized. *Panel A:* control, IC, inspiratory center stimulation, frequency, 50 shocks/sec.; pulse duration, 2 msec.; and voltage, 0.85, 1.5, 2, and 3 volts. PC, pneumotaxic center stimulation, frequency and pulse duration, same as above; voltage, 1.75, 2, 2.5, and 3 volts. Between A and B, meperidine, 3 mg./kg., in 3 doses, was given intravenously. *Panel B:* stimulation of inspiratory center and pneumotaxic center repeated. Parameters same as in panel A.

These results indicate that pentobarbital depresses respiration through at least two possible modes of action. The predominant changes produced by this agent appear to be a prolonged inspiratory phase and a progressive decrease in respiratory amplitude. The same type of prolongation of the inspiratory phase with thiopental has been reported by Brodie,[6] who demonstrated an increase in the duration of burst of inspiratory neurons in the cat. With small doses, the transient nature of this effect is probably attributable to the redistribution of pentobarbital in the body with time, and the consequent lowered concentration of the drug in the blood and brain.

In terms of the concept of the organization of central respiratory mechanisms as proposed in the previous communication,[1] prolongation of inspiration and inspiratory pause would mean that the mechanisms concerned with modulation of the tonically active apneustic center are depressed. The facilitatory influence of the pneumotaxic center on the lower respiratory centers seems to be abolished, as indicated by the

fact that, after 24 to 30 mg./kg. of pentobarbital, stimulation of the former did not result in respiratory acceleration and inspiratory shift.

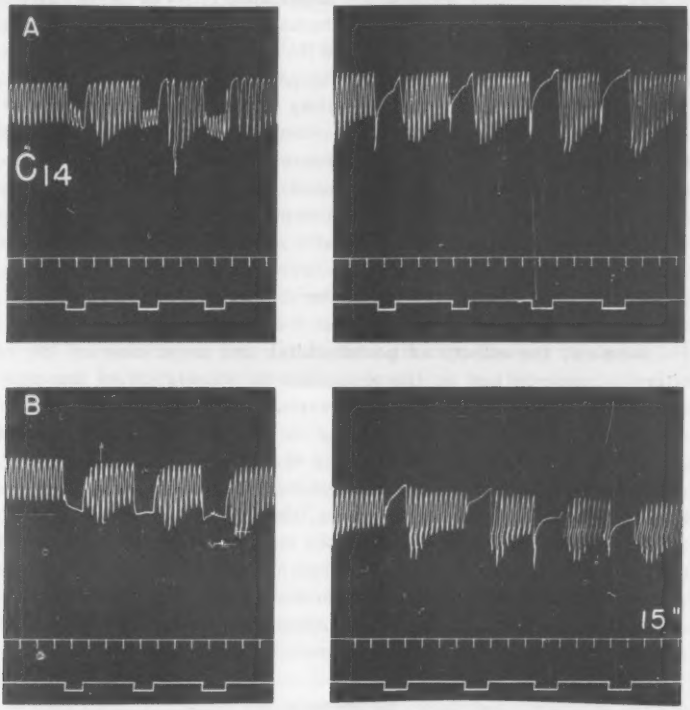

FIGURE 5. Cat 14, 2.8 kg. Midcollicular decerebrate, vagotomized. *Panels A (top row)*, control, central vagal stimulation. *Left panel:* frequency, 10 shocks/sec.; pulse duration 2 msec.; and voltage, 1.5, 2, and 3 volts. *Right panel:* frequency, 200 shocks/sec.; pulse duration, 2 msec.; and voltage, 1.5, 2, 3, and 4 volts. *Panels B (bottom row)*, after 0.5 mg./kg. of meperidine, central vagal stimulation repeated. Parameters same as above.

It thus appears that the multisynaptic feedback circuit between the apneustic center and the pneumontaxic center has been disrupted. On the other hand, the responses to electric stimulation of the central vagus were not significantly altered. However, pentobarbital may still disrupt this modulating circuit through its action on the pulmonary stretch receptors, which have been reported to be depressed by barbiturates in sufficiently high doses.[9]

The progressive decrease in respiratory amplitude indicates that the total activity of the inspiratory center is reduced by pentobarbital. This can be caused by a decrease in the frequency of neuronal discharge or

a decrease in the number of neurons participating, or both. A direct relationship has been suggested between the frequency of inspiratory neuronal discharge and respiratory amplitude.[6,10] The possibility remains, however, that the recruiting mechanism may also become depressed.

Meperidine, on the other hand, exerts its action in a distinctly different manner. The rate of respiration decreased and was accompanied by an increase in the duration of the expiratory pause. The facilitatory mechanism in the pons appears to be depressed, as demonstrated by the disappearance of the acceleratory response to stimulation of the pneumotaxic center and to low-frequency central vagal excitation. At the dose level of meperidine studied, the stimulus threshold of the medullary inspiratory center was elevated, but with supraliminal stimulus, maximal inspiratory response of the same magnitude was obtained. These findings suggest that, when the inspiratory center is activated, it is capable of an output approximately equal to that under the control condition.

In summary, the effects of pentobarbital and meperidine on the respiratory movements and on the responses to stimulation of the pontile pneumotaxic center, the medullary inspiratory center, and the central vagus nerves have been investigated in unanesthetized, decerebrate, vagotomized cats. The results indicate that pentobarbital depresses the modulating and the facilitatory functions of the pneumotaxic center and the inspiratory center in the medulla, thus resulting in slow, shallow respiration with prolonged inspiration. On the other hand, meperidine interferes with the facilitatory function of the pneumotaxic center and vagal afferents. The "integrating" or the "recruiting" mechanisms of the medullary inspiratory center are apparently little affected, and respiration is therefore slow, with an essentially unchanged depth.

References

1. WANG, S. C., S. H. NGAI & M. J. FRUMIN. 1957. Am. J. Physiol. **190**: 333.
2. NGAI, S. H. & S. C. WANG. 1957. Am. J. Physiol. **190**: 343.
3. JOHNSON, F. H. & G. V. RUSSELL. 1952. Anat. Record. **112**: 348.
4. WYSS, O. A. M. 1943. Helv. Physiol. Acta. **1**: 301.
5. HARRIS, T. D. & H. L. BORISON. 1954. Am. J. Physiol. **176**: 77.
6. BRODIE, D. A. 1959. J. Pharmacol. Exptl. Therap. **126**: 264.
7. DUGUID, A. M. E. & R. ST. A. HEATHCOTE. 1941. Quart. J. Pharm. and Pharmacol. **13**: 318.
8. GRUBER, C. M., E. R. HART & C. M. GRUBER, JR. 1941. J. Pharmacol. Exptl. Therap. **73**: 319.
9. WHITTERIDGE, D. 1958. Brit. Med. Bull. **14**: 5.
10. HUKUHARA, T. & H. OKADA. 1956. Acta Med. Okayama. **10**: 151.

DIVISION OF PSYCHOLOGY

INTELLIGENCE, QUANTUM RESONANCE AND THINKING MACHINES*

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Speculation about how the mind works is as old as philosophy itself but, while there is a discernible continuity in the concepts employed to account for the way man perceives and thinks, modern views differ from former theories in at least one important respect. These views are more concerned in what takes place in the brain as a physical apparatus than with what older philosophers called the attributes of the soul. This change in interest began with René Descartes who, while distinguishing sharply between mind and matter, nevertheless located the soul in the brain and, once having conveniently housed it in the pineal gland, left it little to do other than to serve as a sort of detached, albeit divine, observer. Since then the soul has gradually lost even this modest role. To contemporaneous science, how the mind works means how the brain works: such factors as sensation, perception, and cognition are manifestations of brain activity and neural interaction. These are regarded as physical events – events which, as Bertrand Russell (1929) has pointed out, happen to take place in terminal neurons of the central nervous system. Psychology now turns more and more to physics for its ultimate "explanations" of psychic processes.

The subject I shall discuss will concern itself with some of the physical explanations or hypotheses of how the brain works intellectively. More specifically, I shall consider the following two questions. (1) What, in the light of recent advances in neurophysiology and quantum mechanics, is the likely physical event that takes place in the human brain when an individual is said to manifest intelligence? (2) In what way is human mentation as involved in intelligent behavior different from the logical operations performed by thinking machines? In trying to answer these questions, it will be useful to summarize contemporary views on two germane topics. The first is the neurophysiologist's concept of how the brain operates as a physical apparatus and, second, the physicist's concept of *connectivity*.

* This paper was presented at a meeting of the Division on January 18, 1960.

The Division of Nuclear Physics held a meeting on January 13, 1960, at which Richard Ruffine of the Department of Physics, New York University, New York, N.Y., presented a paper entitled "The Three-Body Problem: Electron and Positron Scattering in Hydrogen." This paper will appear in a later edition of the *Transactions*.

A paper entitled "The Design of Underground Shelters for Civil Defense in the City of New York" was presented at a meeting of the Division of Engineering, January 15, 1960, by Guy Panero, New York, N.Y. This article will appear in a later edition of the *Transactions*.

The human brain is now generally regarded as a complex neural network whose main function is to serve as a vast clearing house of incoming and outgoing messages. For this purpose it is conceived of as a complex automatic information exchange or self-regulating intercommunication system. Parts of the nervous system (such as the sense organs) collect information that is then transmitted through synaptic barriers to various centers, although not necessarily fixed loci, where it is eventually integrated. Transmission and integration are achieved through interlacing systems of inhibiting and facilitating reverbatory circuits, and the brain itself has been recently described as a complex of such circuits in continuous activity. A gap unaccounted for in this hypothesis is that much of the received information is unused; one needs to explain what becomes of unused information and, especially, in what manner it is "edited." This hiatus did not present a problem to Descartes, because he provided the brain with a divine editor; the helmsman of modern cybernetics is just another automaton regulating, and regulated by, feedback circuits.

The key work in contemporaneous neurophysiology is integration, generally described as a complex of neural activity or pattern of excitation taking place in or between certain regions of the brain. One of the interesting facts recently demonstrated is that while this organized activity, particularly of the higher functions, such as memory and learning, may be associated with the integrity of certain parts of the cortex, it is not exclusively dependent upon them, since this integration can continue in spite of cortical interruptions. For this reason it has been posited that initiation and regulation of the higher processes may take place and be mediated through regions other than the cortex: for example, parts of the thalamus, various reticular tracts, and other intracephalic communicating systems.

Regardless of where or how integration occurs, however, one is still confronted with the underlying question: To what does this integration correspond and to what can it be equated? Is it a kind of electrical activity that, on reaching a certain level, merely initiates or delimits a particular set of motor responses? Does it represent special cortical patterns that serve to define one or another type of perception? Is it just a state of awareness associated with or defining particular kinds of neural activity? One must distinguish here, as W. Koehler has emphasized, between what a process is and how it is achieved. It is the difference between describing the structure and mechanism of an atomic pile and and trying to account for the fission phenomena in terms of the properties or behavior of the elementary physical particles that produce it. It is the former type of description that now constitutes the physical models of how the brain works (Asby, 1947).

The current definition of the brain that has met with greatest acceptance among neurophysiologists is that it is essentially a screening and

sorting organ, a complex electrochemical servomechanism that in some respects functions like a multiple television system with built-in screening generators and, in others, like a high-speed automaton computer. In either case it is eventually conceived as a thinking or logical machine.

The concept of the mind as a logical machine is not new, but the remarkable achievements of the recently developed digital computers have lent much support to the suggested equivalence between intellectual and computer operations. It is not altogether clear which is the model for which, but that there is strong resemblance between them cannot be doubted.

One of the earliest computers and, perhaps, the only strictly logical machine, that of the English logician Stanley Jevons (1913), was mechanically quite a simple affair. In general appearance it resembled the small upright organ with a keyboard containing twenty-one keys. Sixteen of the keys represented the usual terms employed in logical notations *(A,a; B,b; C,c; D,d);* the remainder designated possible logical operations: for example, one for the copula, one to designate equality, and one for disjunction. To work the machine it was necessary only to press the proper keys designating the signs and letters of the logical proposition and, after thus inserting one's minor and major premises, collect the indicated conclusions by pressing a finis lever. The machine as described by Jevons was not only able to indicate conclusions but would also, to quote Jevons, "detect any self-contradiction between the premises presented to it." The one big drawback and limitation of the machine was that the problems that it solved were primarily those in which only the academic logician was likely to be interested. The modern automaton is infinitely more versatile (and more complex), but deals with many problems that even an average bank clerk or business executive can understand. It can perform many more practical operations. It is a computer, not a logician.

The remarkable tasks that electronic computers can achieve are now fairly familiar. These machines perform complex calculations, solve differential equations, compute trajectories, and unravel codes. They can store information of a complex nature and give it back at a moment's notice. The latest models of the digital computer can do many things that have hitherto been considered purely mental or restricted to human capability. With proper programing such a machine can be made to exhibit retention and recall, make alternative choices, check its own mistakes (which it seldom makes), translate Russian into English and, if put to it, play a fair game of chess. However, for all these remarkable "abilities" it lacks certain basic potentials of which only man and certain animals seem potentially capable. The automaton computer cannot initiate action, or profit from experience, without external intervention. It can do only what it is told to do: that is, what has been built into it. The most important limitation of the computing automaton however, is that while

it can do things, it cannot understand them; it has abilities, but these abilities do not go beyond performance.

The basic distinction between intelligence and abilities, namely, that of understanding as against merely performing a task, is the crux of the matter. There is no doubt that machines can now be designed and have already been constructed that manifest mental abilities of various sorts including that of logical reasoning. However, for the same reasons that abilities cannot be equated with intelligence, the electronic automaton cannot serve as a model for it. What is needed is a conceptual scheme that would yield some insight into the functioning of the brain, not only in terms of its individual components but also collectively, as a unit, as well. It is here that the physicist's construct of *collectivity* offers a promising lead.

The physical concept of collectivity is derived from the particle-wave duality of quantum mechanics, which was so well elucidated by Niels Bohr's complementarity principle, which aims to reconcile the contrary aspects of the (dual) behavior of the elementary particle. These are its wave and particle characteristics which, although they cannot be observed simultaneously, together form a complete description of the behavior of the basic entities present in nature. This duality of behavior is ascribed not to the intrinsic properties of the elementary particle, for example, the electron, but to its interaction with other particle congeries or systems, such as the apparatus used. The elementary particle is thus conceived of as being capable of manifesting two types of behavior: one in which it acts, as it were, alone or independently, and another in which it acts communally or collectively. Contemporary physics teaches that the properties of molecular and atomic systems arise essentially from their interaction or their contiguous presence.

What seems to characterize the behavior of the elementary physical particle might give us a key for understanding the elementary units involved in neural activity. One might reasonably assume that the individual neurons of the nervous system, like the electrons of the atom, may have a collective as well as an independent behavior. When we say neurons we mean, of course the fine particles in the neurons and particularly those in the cortical cells. However, the important thing to be emphasized is that there is a collective as well as an individual behavior of the neuron cells and that the characteristics of this behavior are due to interaction processes and not merely to the inherent properties of neural protoplasm.

In light of the foregoing I venture the hypothesis that all mental processes, including those of consciousness and cognition, are manifestations of collective behavior of the elementary systems in the encephalon. Different spatial and electrochemical field patterns define various psychological processes, and these are aroused or constituted when they attain a sufficient intensity due to the collective activity of the generated

behavior. This activity may be manifested externally either as various kinds of electric rhythms in the form of short-lived waves (EEG, alpha, and beta) or, as recently shown, by less fluctuating or so-called quasi-steady currents.

We now come to the possible physical equivalent of what we have termed insightful or intelligent behavior: namely, the event or the events that take place in the brain when an individual may be said to perceive, is aware of, or educes a relation. Note that I have said, again, equivalent and not a correlate of: I look upon perception, cognition, and insight not as concomitant physical events in the brain, but as the events themselves. These events are at once both mental and physical. They are different only in the way they are described.

With the foregoing as a point of departure, it would seem that insight as a physical fact could be intelligibly described as a collective response of the elementary systems in cortical cells in one or another region of the brain. This interaction must be conceived as occurring not through the transmission of impulses, in the manner classically postulated, along axons or nerve trunks, but rather as a *resonance* phenomenon.

The resonance with which we are most familiar is the kind manifested in the re-echoing of sounds through reflection or its prolongation through reverberation. It is the response of a system or object, such as a tuning fork, having a given vibrating frequency to another periodic stimulus or vibration of the same or nearly the same frequency. Similar phenomena characterize the reinforcement and impedance conditions of electric circuits, but perhaps what would be immediately pertinent for our conceptualization of mental processes are the behavioral properties of the individual elementary particle. One of the most important of these is the property of *quantum* mechanical *resonance*. The quantum mechanical resonance of an elementary system differs in a basic respect from the performance of macroscopic bodies such as, for example, the prongs of a tuning fork. In the latter, the reinforcement of sound vibration results from a simple addition or superposition of one series of amplitudes onto that of another. In the case of quantum mechanical resonance, "the separate wave components are no longer considered as existing independently. The resultant amplitude formed by superposition of other states is not a simple sum of the amplitudes of the interacting components. The wave interaction of one set of particles with another results in a new state or system" (Stern, 1956).

In the light of the foregoing I suggest that mental events in the brain consist of the creation of successive molecular systems when activity in any one group of cells is reinforced or inhibited by the reverberation to particles in some other group of cells. Mental phenomena are patterns of such resonances, or recurring quantum mechanical systems, activated in one or another part of the brain. Insight is the perception or psychological equivalent of a certain type of resonance: the type that happens

to have meaningful implications for the individual experiencing it. Intelligence is a sequence of such insights leading to purposeful or practical behavior. An intelligent person may thus be defined as one who has been endowed with more or better resonators. This does not exclude the possible influence of environmental stimulation, but it does support the view of Paul Weiss that any pattern of behavior "is developed by the laws of its own embryonic differentiation without aid of sensory input from the outside world."

Two additional remarks are required. First, whatever the nature of the physical process, the phenomena must be understood as occurring initially at a molecular and not at a macroscopic level. To be sure, they may be later amplified macroscopically. Gross stimulation of the brain, or damaging it, as by cutting or extirpation, while capable of furnishing useful information to the neurologist, is of little value in telling us what is taking place in the brain. By the same token, attempts at altering its function will depend more on how we can modify its molecular structure. For this reason electric and chemotherapies, in spite of their negligible contributions to date, hold out much more hope for effective change of human behavior, but not necessarily for the better, than do psychological procedures. However, the chemotherapies of the future, of course, may necessarily involve techniques quite different from those presently in vogue.

The second remark to be made concerns thinking as a psychological phenomenon. The so-called laws of thought, as Bertrand Russell has pointed out, are not descriptions of psychological processes, but only a set of rules for testing the validity of logical propositions. Human thinking only occasionally follows such rules. As introspectively described, valid thinking is more generally achieved through sequential associations and sudden insights than by logical analysis. At times thinking is also evaluative, that is, it involves judgments as to the appropriateness, desirability, and usefulness of its conclusions. In such instances it is also intelligent.

The answer to the question as to whether machines can think does not, of course, depend solely on the manner in which they achieve their end, nor is it necessarily tied to any specific hypothesis (Wisdom, 1956): for example, the hypothesis that the chief mechanism of the central nervous system is one of negative feedback. The brain may or may not function predominantly in this way.

Nevertheless, if by thinking one comprehends primarily the capacity to process, sort, and utilize information, to execute logical operations, and to solve rational problems, one must agree that machines can think. One is forced to this conclusion, not only from an appraisal of the tasks that the digital computers are already known to perform, but also from the theoretical considerations of their potentials as described, for example, by Norbert Wiener, J. von Neumann (1951) and A. M. Turing (1951).

However, while I have been convinced that machines can think, I find no indication that they are capable of any type of a performance that I call intelligent. My chief reason for this view is, as I have already indicated, that while the digital computer can do many things that have previously been considered characteristic of human mentation, the abilities manifested do not go beyond performance. Although capable of making decisions, the digital (or analogue) computer cannot evaluate its own work, that is, understand either the relevance or purpose of what it is doing. It may be able to solve complex differential equations but will not, unaided, set up a simple experiment. It will go on calculating if its house is on fire or the problem it is trying to solve is no longer relevant or necessary.

We have just conceded that machines can think and, we may add, that they can make decisions. However, these decisions are always statistically determined: that is, they depend on the totality of combinations that the input information makes available. Once the computer has been programmed, it must go through a predestined routine. Compared to the human mind, it may have to do an inordinate amount of work even in solving a simple problem. The fact that it can perform it very much faster and more accurately does not make it intelligent. Intelligence, like creativity, presupposes avoidance of what Henri Poincaré (1951) has termed "sterile combinations," that is, combinations that in the long run are irrelevant and useless. "The inventive individual," he once said, proceeds not "like a purchaser before whom are displayed a large number of samples, and who examines them one after another to make a choice; here the samples would be so numerous that a whole life would not suffice them . . ." Actually, "the sterile combinations do not even present themselves to the inventor."

Thus far, it will have been noted, I have not offered any succinct definition of intelligence, although the title of this paper indicates that I should attempt to formulate one. I have refrained from doing so, not only to avoid dilating on a construct about which there is so much disagreement, but because I have hoped that my own concept of intelligence might be inferred from the context in which I am using the term. I have presented elsewhere a formal definition of intelligence that may or may not be better than others that are more familiar. Space is lacking to discuss the latter, and I do not think that my own concept of it would settle matters. In concluding, therefore, I shall state only what I think intelligence is not, and I shall designate the one attribute which in my opinion, is its *sine qua non*. Intelligence (Wechsler, 1958) however defined, is not the equivalent of any ability, however esteemed, particularly not of learning or even of abstract reasoning ability. Something more than performance must be involved. That something, as I have already indicated, is awareness of the meaning and purpose of performance on the part of the operant. I have called this aspect of intelligence understanding.

Behavior that does not involve understanding is in my opinion not intelligent. Machines do not possess understanding; hence, by my definition, they are essentially stupid or, they are at best, idio-savants.

Digital computers may be able to think, to learn, and eventually, perhaps, also to reproduce themselves; but they cannot understand what they are doing. In this respect they may not differ very much from the way human beings function much of the time; all of which may mean simply that men usually behave like machines. However, sometimes they do not; and then they build machines.

References

ASHBY, W. R. 1947. The nervous system as a physical machine. Mind. 56: 44-59.

JEVONS, W. S. 1913. The Principles of Science. 2nd ed. Repr. London, England.

NEUMANN, J. VON. 1951. General and Logical Theory of Automata. Cerebral Mechanisms of Behavior. L. A. Jeffress, Ed. Wiley. New York, N.Y.

POINCARÉ, H. 1951. Mathematical Creation. The World of Mathematics. 4. J. R. Newman, Ed. Norton. New York, N.Y.

RUSSELL, B. 1929. Mysticism and Logic. Schuster. New York, N.Y.

STERN, A. W. 1956. The Nature of G and the Concept of Intelligence. Acta Psychol. 12: 282-289.

TURING, A. M. 1951. Can a Machine Think. The World of Mathematics, J. R. Newman, Ed. Norton. New York, N.Y.

WECHSLER, D. 1958. The Measurement and Appraisal of Adult Intelligence. Williams & Wilkins. Baltimore, Md.

WISDOM, J. O. 1951. The hypothesis of cybernetics. Brit. J. Phil. Sci. 2; 2; 1956. General Systems. 1: 111-112.

DIVISION OF ANTHROPOLOGY

SOME RECENT DEVELOPMENTS IN THE SOCIOLOGY OF THE BAMBUTI PYGMIES*

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A striking feature of any survey of ancient and early sources concerning the African Pgymies is that from the time these people first entered the recorded scene, in Fourth Dynasty Egypt, our knowledge of them steadily decreased until the late Nineteenth Century.

To the mediaeval European world the Pygmies were no longer the reality they were to the ancient world; they had already become a myth. So much so that one great Seventeenth Century English scientist, E. Tyson, obtained a skeleton and wrote a treatise entitled *The Anatomy of a Pygmie Compared to That of a Monkey, an Ape and a Man*, in which he proved conclusively that the legendary Pygmy was nothing but an ape. The skeleton survived, and when examined later it was realized that Tyson was not so far wrong – it was that of a chimpanzee.

In the latter part of the Nineteenth Century explorers such as H. Stanley and G. Schweinfurth gave the first detailed, sober, eyewitness accounts of Pygmies to the modern world, but it was not until the 1930s that any scientific work was undertaken. In 1929 Paul Schebesta made the first of a series of field trips to the Ituri Forest, and it became established that this area in the northeast corner of the Belgian Congo was the last stronghold of the true African Pygmies, whom he calls "Bambuti," although groups of Pygmoids appear in a number of other parts of the equatorial belt.

Schebesta's findings over a number of years, as published by him in his major work *Die Bambuti Pygmaen vom Ituri*, remained largely unchallenged except for a few relatively small details. The work of other anthropologists such as B. J. Costermans and M. Gusinde tended with some exceptions to confirm his findings, and certainly his interpretation of the Pygmy-Negro relationship has been widely accepted, supported as it is by almost every traveler's account.

Following my second visit to the Ituri Forest in 1954, I found myself sharply in opposition to Schebesta, and continued to find not only my interpretation but also my facts almost invariably divergent from his. At first it seemed that there could scarcely be room for both accounts, that one of them must be seriously mistaken, but after my third visit, in 1957 and 1958, at the end of which I had the opportunity for meeting Schebesta in Vienna, Austria, and discussing the whole problem with him, it appeared

*This paper was presented at a joint meeting of the Division of Anthropology and the American Ethnological Society on January 25, 1960.

that each of us in his own way was correct, because each had unknowingly been forced into observing from totally different viewpoints.

Our major point of departure was over the nature of the relationship between the BaMbuti and the various Negro tribes with whom they associate. Following this, we disagreed over the practice and significance of certain rites, and to a much lesser extent over the social organization of the BaMbuti.

Schebesta was of the opinion that the BaMbuti were not "degenerates" of Negro stock, as some had maintained, but both racially and culturally distinct. He devoted a great deal of research to showing that the magico-religious system of the Pygmies, although outwardly similar to that of the Negro tribes, is in fact quite distinct. With this I completely agree. However, at the same time he claimed that the Pygmies, who are nomadic hunters and gatherers and the original inhabitants of the forest, had fallen under the yoke of the invading Negro tribes and were in fact subject to them.

The Negro, according to Schebesta, was able to exert control over the Pygmies, to force them to work on his plantations, or to act as hewers of wood and drawers of water; perhaps most important of all, he was able to use them as hunters to bring him his supply of meat. In return for this he supplied the Pygmies with plantation products and with metal weapons and utensils. An essential characteristic of this relationship, as described by Schebesta, was the dependence of the Pygmies on the Negroes, their inability to survive on their own resources.

Schebesta cited, as an example of the high degree of this dependence, the *nkumbi* initiation rite practiced by a large group of the forest Negro tribes. In this initiation boys between the ages of nine and twelve are circumcised, then initiated into the adult mysteries of tribal lore. They acquire privileges and responsibilities in this way. The Negroes, according to Schebesta, assert their authority over the Pygmy by initiating him together with the Negro boys, generally sending the Pygmy first "to clean the knife." It forms a special bond between the Pygmy and the Negro boy initiated next to him, involving mutual responsibilities. However, it also subjects the Pygmy to Negro tribal lore and supernatural authority, and so places him more than ever in a subservient position.

To the Negro it is inconceivable that any boy should grow up into adulthood without being initiated, and he assumes that the Pygmies feel the same compulsion. Only the Negroes have the ritual specialists qualified to perform the ceremony, however, and in this way they feel that they have ultimate control over the BaMbuti. They also assume that the Pygmies, once initiated, will be subject to the same supernatural authority that rules over them and that, even if they do not accept the tribal code, they will be punished for any disobedience, having placed themselves, by participation in the *nkumbi*, under that authority.

I have evidence that in one area, and I suspect in many others, if not all, this is only true as a picture of what the Negro believes, and of what the Pygmy appears to believe if he is observed directly in relationship with the Negroes, not only in the villages but even in the forest when still in the company of Negroes. I think it would have taken longer than it did to realize the true nature of the relationship had it not been for the fortunate opportunity I had in 1954 for witnessing an exceptional *nkumbi* in which no Negro boys took part, as there were none of a suitable age. This has been fully described by me elsewhere (1957); here I need give only the main outline.

The initiation took place in the Epulu district of the Ituri Forest; it had been delayed for some months in the hopes of persuading at least one Negro boy to take part, but his father was a Christian and refused permission. Eventually the Negroes decided to proceed, as they felt the *nkumbi* must be held, three years having passed since the last one. The entire procedure was exactly the same as if it had been for Negro boys, the Negroes bearing the brunt of the expense, the Pygmies supplying a small amount of labor and some meat for the feasting. The important difference was that, by their own custom, no Negro was allowed to stay in the initiation camp overnight – only relatives of the boys initiated had this right. To the Pygmies, however, this rule was of little significance. As far as they were concerned, any Pygmy male was welcome, and they invited me to stay as well, knowing that I was interested and that I would keep them well supplied with tobacco and other luxuries. The Negro attitude was ambivalent – they knew me well enough, and felt that they too might benefit by my presence, but at the same time they were envious of my apparent immunity from the supernatural sanction that they felt would strike them down if they flaunted custom as I did.

I was allowed to stay, however, and so was able to see firsthand the extraordinary duality that is, I believe, the major characteristic of the Pygmy's relationship with the Negro. As long as one or more Negroes were present, as was almost always the case from dawn to dusk, the Pygmy boys and their "fathers" observed all the various prohibitions and behaved with the appropriate respect toward sacred emblems, and the children displayed the fear expected of them when they heard the sound of the bull-roarer and were told it was the voice of a dangerous and powerful spirit. However, at night, when all the Negroes had left, the initiation camp was transformed. The "fathers" complained openly in front of the boys about the, to them unnecessary, brutality of the Negroes, and equally openly made fun of the Negro conviction that the Pygmies believed all that "nonsense" about bull-roarers, sacred emblems, and other such tenets.

The boys themselves not only broke any and all prohibitions after the Negroes had left, but joined in the fun, miming Negro antics even to the swinging of the bull-roarer that they were meant not to have seen.

Some of their "offenses" were willful and deliberate, such as the way they used to play punchball with a sacred banana that hung from the roof of their hut; others were merely incurred in behaving in what was to them the most reasonable way – by eating with their parents, by eating prohibited foods, by washing in the rain to get rid of the white clay smeared on their bodies during the day, despite the Negro teaching that to be touched by rain means death to an initiate.

By their actions and by their conversation it became quite clear that the Pygmies took part in the *nkumbi* simply in order to acquire status in Negro society, without accepting any of the magico-religious implications. They certainly did not feel themselves bound by the supernatural sanctions that bound the Negro to such a point that he could not even properly supervise the *nkumbi*.

Most significantly, however, these same boys who acquired the status of adults in the Negro village in this way were still considered as children when they returned to their forest hunting camp. They returned to their mothers, were not allowed to take part in the adult male religious singing activities (the *molimo*) and, in fact, reverted to their former status without any change. This led me to suspect that there might be dichotomy of values, a hiatus between the forest and the village life of the Pygmy. Strong evidence that this was so appeared immediately in an examination of the music of the people.

Here again Schebesta and I had found ourselves in contradiction or, to be more exact, we had found that our facts were in apparent contradiction. His observations were that the Pygmies were poor musicians, specializing in drumming and wild dancing. My own observations were that the Pygmies were excellent musicians who never used drums and who had the most exquisite and even delicate sense of dance. The reason for our disagreement, I suppose, should have been clear before, but it now became increasingly evident, namely that Schebesta's observations had been made almost entirely, and of necessity, either of Pygmies in Negro villages or in forest camps where Negroes were present, whereas mine had been made, apart from the *nkumbi*, mainly in the forest. Under the one set of circumstances the Pygmies behave in one way, and under the other in a completely different way. There is in fact a barrier, consciously felt by the Pygmies and maintained by them, keeping the two worlds apart.

My major field trip, in 1957-1958, was spent almost entirely in the forest and with no Negroes present. The first and most obvious difference noticeable between forest life and village life, apart from economic activity, was in music. The forest songs of the BaMbuti were never sung during the occasional short visits to the village. Drums were used only when they were within easy reach of a Negro village from which they could be borrowed or stolen, and they were never used on any important religious occasion. Even more significant, it became apparent

that the Pygmies consecrate any particularly important event with a special kind of praise song. At the same time it was equally apparent that Negro rituals and customs that the BaMbuti practiced in the village were of no significance in the forest, were not practiced there, and were not consecrated in this way. For the *nkumbi*, for instance, the Pygmy has no music of his own; he merely imitates the Negro.

The importance of this can be recognized only when it is known how important song and dance are to the Pygmy in his forest life. It is then that the hiatus between the two worlds, consciously and deliberately maintained, becomes most striking. By refusing to consecrate village activities with forest music, or at least by refraining from doing so, the BaMbuti deny Negro rites any validity in the forest. Thus the elaborate funeral and mourning ceremonies that the Pygmies go through if one of their members dies when in a Negro village, or the marriage ceremonies, or even the *nkumbi* itself, are in no way related to their forest life. Conversely, the Pygmies will not profane their forest life by bringing it to the village, which explains why Schebesta did not hear their forest songs, for they will not willingly sing these even in the forest if Negroes are in the camp.

In this way the BaMbuti maintain a dual system of behavior and values. In the forest they live one way and are bound by certain values; in the village they live another life. This opposition is even formalized in the course of forest celebrations of the *molimo*, a religious festival occasioned, among the Pygmies, by any major crisis. This festival, which I describe fully in one of two articles about to be published in *Zaire*, consists mainly of the singing of special *molimo* songs to the forest. The purpose of all forest music, among the Pygmies, is "to rejoice the forest." Thus a girl at her first menstrual period sings "to rejoice the forest" in appreciation of the fact that she is now a potential mother, and this is an occasion for great rejoicing. Similarly, hunting songs or honey-gathering songs are sung "to rejoice the forest" with typical Pygmy logic and realism when there is any adverse crisis such as illness, severe bad hunting (a rare occurence), or death.

I shall not dwell here on how divergent this is from Negro practice in the Ituri area, where to the cultivator the environment is hostile, where there is little to be thankful for and a great deal to give rise to accusations of sorcery and the practice of witchcraft. Suffice it to say that the Pygmies, as distinguished from the Negroes, do not consider illness, death, or misfortune in any form as the results of human or supernatural acts of hostility. Their reasoning, to paraphrase their own accounts, is that normally the forest supplies all their needs and is therefore good. They refer to the forest as father or mother, because it looks after its children (the BaMbuti). It is normal for life to be full and satisfactory, without illness or misfortune. Hunting accidents are extremely rare, as are attacks by wild animals. The dangerous time is

at night, when sleeping. At such a time animals may enter the camp, or the camp may be attacked by hordes of army ants, or other things may happen that may be avoided during the day. So the Pygmy says that any misfortune, whatever it may be, must be attributed to the fact that "the forest is sleeping." The obvious remedy is to wake it up, and this is the purpose of the special *molimo* songs, in which a long wooden horn is used to echo the song far into the depths of the forest, so that it is sure to awaken. The songs do not ask for this or that; many of them are almost completely without words, mere vowel sounds improvised at the whim of each individual. However, the song is a corporate effort in which all adult males are expected to take part. Once the forest is awake, it is reasoned, then everything will come right again. As one song says, "If darkness is (or must be), the darkness is good" – that is, death is accepted, along with other misfortunes, either as the will of the forest and therefore good, or as a result of the failure of the Pygmies to wake it up in time.

The *molimo* is carried out with little ceremony, although it involves, among other things, nightly feasting. Before the great *molimo* songs are sung; especially if the camp is anywhere near a Negro village, someone will quietly drag a few branches or fallen logs across the path leading to the village, blocking it off, shutting out the profane world outside the sacred forest. I have seen the performance of a *molimo* temporarily halted by the presence of one Negro in the camp. At other times I have seen "mock" performances when some important Negro insisted on attending in order to pay his respects to the dead.

This opposition of the Pygmies, which I think can be fairly compared with the opposition of sacred and profane, repeats itself and characterizes all Pygmy relationships with their Negro neighbors. However, it is evident only if you observe customs from both sides of the barrier, and this is not easy. Schebesta observed from one side, and was cut off, without knowing it, from the other. Similarly I observed from the Pygmy side, and was consequently *persona non grata* among the Negro tribes. By putting the two inescapable sets of facts side by side one obtains a much clearer and fuller picture. With this in mind, it is much easier to understand the Pygmy-Negro relationship that has been the source of much misunderstanding and doubt.

Outwardly, from the village point of view, the Pygmies are a subject people, subjecting themselves to Negro masters and to the control of Negro supernatural sanctions. The Pygmies work, either on plantations or as hired hunters, in return for plantation products such as rice, plantains, and manioc, and for certain metal artefacts. They seem to have adopted not only the language but also the culture of whatever tribe they happen to associate with; from the forest point of view, however, it is just the reverse – the Pygmies are masters of the situation. They are free to come and go as they please, and it is a fact that no

Negro can force a Pygmy group to act against its will, except in so far as he can bribe them. The moment a Pygmy group becomes dissatisfied it will return to the forest, and even attach itself to a different Negro group. This is in fact a not infrequent source of dispute between Negro groups and individuals, who claim "hereditary ownership" over Pygmy groups or families.

It is also a fact – one accepted with some reluctance by any Negro who "owns" Pygmies – that the latter will take from the plantations whatever they feel is their due if they are not given it. It now seems evident that the Pygmies accept the outer trappings of Negro custom only for what they are worth to them, and do not feel themselves bound by Negro law or supernatural sanction in consequence. A Negro-supervised funeral and mourning ceremony does not relieve the Pygmy of the necessity for holding a *molimo* if he feels that a particular death calls for it. Nor does a Negro-controlled marriage between two pygmies, with the exchange of gifts and payment of wealth, make the marriage any more stable or prevent the two from separating when they return to the forest, leaving the Negro "masters" to make the necessary restitution.

The more the Pygmy gets used to such products of the Negro community as food, iron, clothes, tobacco, and palm wine, the more, of course, will he find himself obliged to come into increased contact with the village and, as luxuries become necessities, so will he become increasingly dependent on the Negro, although present administrative measures to force Pygmies to cultivate plantations are likely to alter the entire situation in a drastic and possibly tragic manner.

The key to the present situation, in my opinion, is to be found in a comparison of a Pygmy group when in the forest with that same group when in the village, with particular attention to its system of values. The evidence thus far reveals the barrier that, I suggest, is formalized in the ritual closing of the path leading to the village during the *molimo* and by the refusal of the Pygmies to sing the sacred forest songs in the profane Negro village. Such a comparison would certainly also reveal the small amount of control, natural or supernatural, that the Negroes exercise over "their" Pygmies and the ineffectiveness of the alleged system of inheritance.

In case there should be any doubt as to Pygmy opinion regarding their relationship with their Negro neighbors, I conclude by quoting a wise old MaMbuti who said to me, in explaining why Pygmies resort to all sorts of tricks to keep the Negroes away from the forest: "This is our forest; it is a good forest, and it is no place for savages."

References

COSTERMANS, B. J. 1937. De Efe van Watsa-Gombari. Congo II. :526-532.

COSTERMANS, B. J. 1938. Torè, God en geesten bij de Mamvu en hun dwergen. Congo I. :532-547.

GUSINDE, M. 1942. Die Congo Pygmäen in Geschichte und Gegenwart. Acta Nova Leopoldina. 76.

GUSINDE, M. 1948-1949. Urwaldmenschen am Ituri. Springer Verlag. Vienna, Austria.

GUSINDE, M. 1956. Die Twiden: Pygmäen und Pygmoide im Tropischen Afrika. Wilhelm Braumüller. Vienna, Austria.

JOSET, P. E. 1948. Buda Efeba. Zaire I, 25-40; 137-157.

SCHEBESTA, P. 1933. Among Congo Pygmies. Hutchinson. London, England.

SCHEBESTA, P. 1936. My Pygmy and Negro Hosts. Hutchinson. London, England.

SCHEBESTA, P. 1937. Revisiting my Pygmy Hosts. Hutchinson. London, England.

SCHEBESTA, P. 1938-1950. Die Bambuti Pygmäen. Inst. Roy. Colonial Belge. Brussels, Belgium.

SCHEBESTA, P. 1952. Les Pygmées du Congo Belge. Inst. Roy. Colonial Belge. Brussels, Belgium.

SCHMIDT, W. 1910. Die Stellung der Pygmäenvölker in der Entwicklungsgeschichte des Menschen. Strecker & Schröber. Stuttgart, Germany.

SCHMIDT, W. 1933. Der Ursprung der Gottesidee: Band IV: Die Religionen der Urvölker Afrikas. Achendorffsche Verlagsbuchhandlung. Münster, Germany.

TURNBULL, C. M. 1957. Initiation Among the Bambuti Pygmies of the Central Ituri. J. Roy. Anthropol. Inst. 87(2).

TURNBULL, C. M. 1959. Legends of the Bambuti. J. Roy. Anthropol. Inst. 89(1).

DIVISION OF OCEANOGRAPHY AND METEOROLOGY

ARCAS HIGH-ALTITUDE METEOROLOGICAL ROCKETSONDE SYSTEM*

John A. Brown

Ballistics Research Laboratories, Aberdeen, Md.

The Arcas rocket shown in FIGURE 1 (all-purpose rocket for collection of atmospheric soundings) originally was developed under the sponsorship of the three services as represented by the Office of Naval Research, Air Force Cambridge Research Center, and the United States Army Signal Research and Development Laboratories. The Arcas sounding rocket was developed for the stratospheric meteorologist and high-altitude research scientist as a low-cost integrated system to obtain routine temperature and pressure and wind measurements, and to conduct experiments between 80,000 and 250,000 feet.

Vehicle Discussion

The current Arcas rocketsonde system consists of the following seven components:

(1) *Propulsion.* A high-impulse, solid-propellant rocket motor supplies the thrust for the Arcas sounding rocket. The high-energy aluminized rocket fuel is designed as an end-burning grain that supplies thrust for a relatively long time.

The long-burning time of this propellant-charge design permits a higher degree of conversion of propulsive energy into rocket velocity and performance than is available in comparable sounding rockets. A greater portion of the time of the rocket thrust is used in the higher regions of the atmosphere, and a minimal amount of thrust is lost because of aerodynamic drag.

The end-burning Arcas motor makes possible a higher propellant-loading density and a vehicle slenderness for minimal drag – thus, the smallest vehicle for a given peak-altitude attainment.

As shipped, the Arcas motor is ready for immediate launching after igniter insertion. The motor is supplied with an easily attached, electrically actuated igniter requiring a current of only 2 amp. for reliable operation.

(2) *Aerodynamic performance.* The Arcas is designed to carry a 12-lb. payload to an altitude of 210,000 feet. Modification in peak altitude can be made by varying payload weight. The rocket is aerodynamically stable with payloads as light as 5 lb. With a 12-lb. payload, the Arcas reaches a maximum burnout velocity of 3700 ft./sec. at 47,000 feet.

* This paper, illustrated with slides and motion pictures, was presented at a meeting of the Division on January 26, 1960.

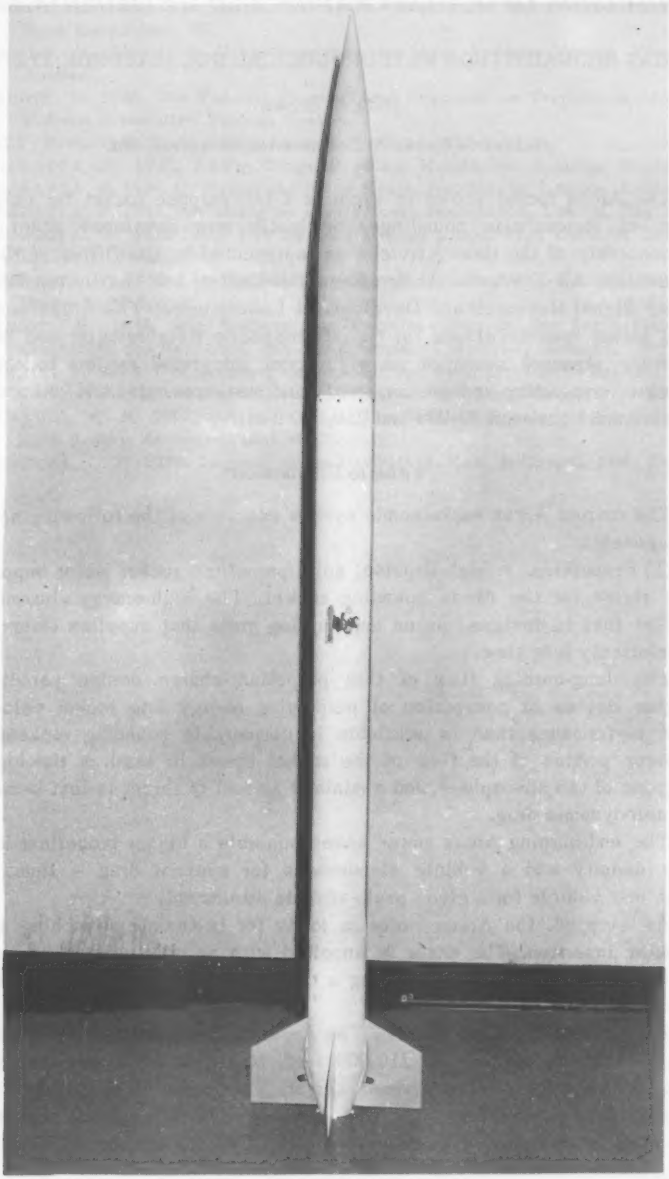

FIGURE 1. The Arcas high-altitude rocketsonde.

Four tail fins are attached to the motor-tube boattail for aerodynamic stability. Fins are aligned to maintain rocket roll rate below a maximum of 2 rps.

TABLE 1 and FIGURE 2 show the performance data for the Arcas rocket.

TABLE 1

PERFORMANCE DATA

Nominal payload (including parachute recovery unit)	12 lb.
Maximum altitude	210,000 feet
Time to maximum altitude	128 sec.
Altitude at burnout	47,000 feet
Maximum velocity	37,000 ft./sec.
Acceleration at launch	30 g.
Launch velocity	125 ft./sec.
Total rocket weight (including payload)	77.0 lb.

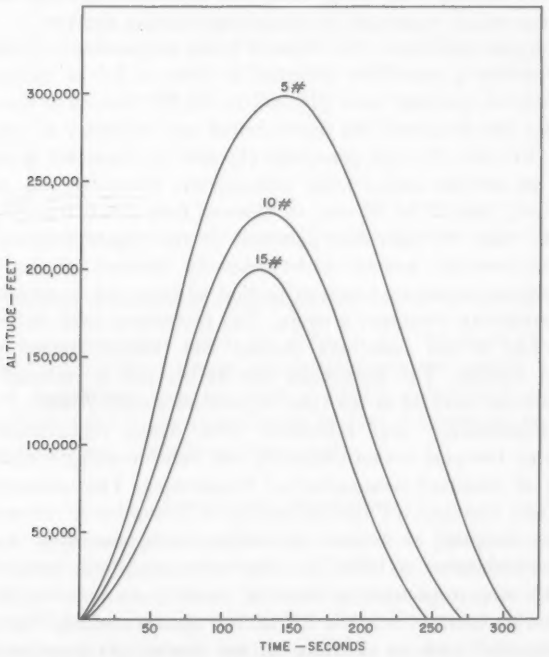

FIGURE 2. Arcas trajectory-vertical launch (5-, 10-, and 15-lb. payloads).

(3) *Arcas launcher.* A unique, closed-breech portable launcher has been developed to launch the Arcas easily and accurately. Utilizing the initial exhaust gas pressure built up by the rocket, the launcher expels the rocket at a velocity higher than could otherwise be achieved. Rocket trajectory dispersion is thus reduced and the accuracy of impact-point prediction is improved. Aiming within a 20° vertical cone is accomplished by means of azimuth and elevation adjustment.

The launcher is designed for easy assembly so that launching may be carried out from shipboard and remote locations as well as at established missile ranges. The launcher consists of 5 major parts weighing a total of 390 lb. Two men can assemble the launcher in approximately 2 hours.

(4) *Payload separation.* To ensure positive separation and deployment of the Arcas payload and recovery parachute at peak altitude, a pyrotechnic timing device and separation charge are used with the standard Arcas rocketsonde system.

At burnout of the propellant charge, the timing device is initiated so that, after a predetermined delay, the separation device is ignited. Separation of the parachute and instrument payload from the rocket motor is accomplished with a relative velocity of 50 feet/sec. and a maximum acceleration of 50 g. The timing delay and separation devices are located between the rocket motor and the parachute-housing section.

(5) *Parachute recovery.* The standard Arcas meteorological rocketsonde system employs a parachute designed to lower a 6.5-lb. meteorological instrumentation payload from 210,000 to 80,000 feet at a descent rate sufficiently low to permit the measurement and telemetry of meteorological data (FIGURE 3). The parachute (15 feet in diameter) is aluminized in order to provide better radar reflectivity. Normally, the instrument package will take 25 to 30 min. to descend from 210,000 to 80,000 feet.

(6) *Nose cone and parachute sections.* In the standard Arcas meteorological rocketsonde system with parachute descent of the payloads, instrumentation is secured to a plate that adjoins and is attached to the forward parachute container closure. The instrument load and nose cone are attached to the parachute through the instrumentation plate and parachute closure. The nose cone can be ejected or retained with the instrumentation payload at the time of parachute deployment.

(7) *Instrumentation and telemetry.* The Arcas rocketsonde system incorporates low-cost rocket telemetry and radio-tracking instrumentation operating at standard meteorological frequencies. The telemetry system (AN/DMQ-6) consists of the following: a motor-driven commutator for sequential sampling of various parameters being measured; a blocking-oscillator modulator; a 1680 Mc. FM cavity-oscillator transmitter; and a 403 Mc. superregenerative detector receiver to receive the ranging modulation transmitted from the AN/GMD-2 ground station. The nose cone can be tracked both on the way up and during the parachute payload descent with a ground station Rawin set AN/GMD-2. As an alternative

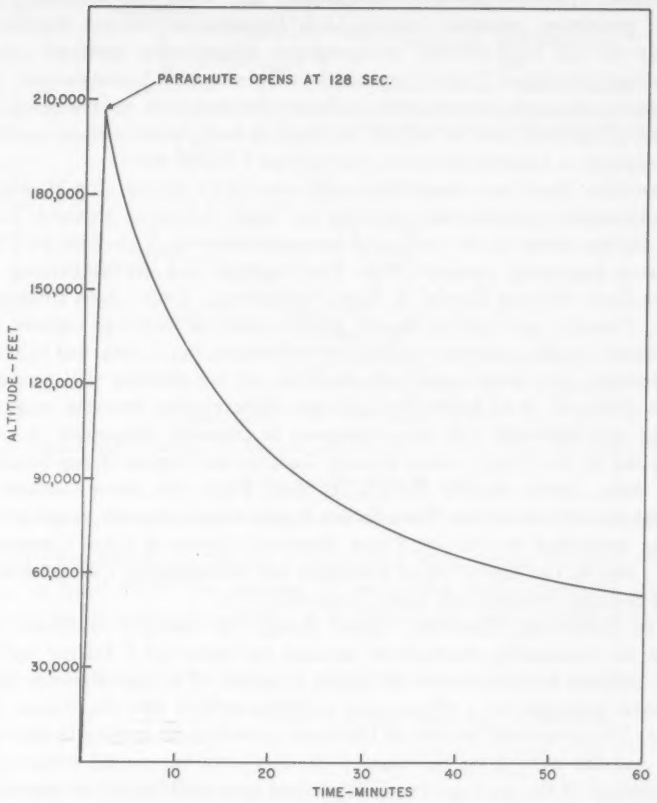

FIGURE 3. Descent of Arcas parachute with 6.5-lb. package.

measure, a ground-based radar set FPS-16 can be used for position tracking and a AN/GMD-1 Rawin set for telemetry. At present a modified AN/AMT-4 radiosonde together with a GMD-1 ground set and FPS-16 radar are used in the Arcas rocketsonde system at launching areas where the newer ground set (GMD-2) is nonexistent.

Atmospheric Parameters

Presently only two meteorological parameters are being directly measured by the Arcas rocketsonde system. These are temperature and wind measurements. However, since a reliable trajectory altitude can be obtained by radar or through the use of a GMD-2 ground set, a reliable pressure versus altitude may be computed by means of the perfect gas law and the hydrostatic equation.

Several types of pressure instruments are under development. The most promising pressure sensor is a hypsometric device similar in design to the high-altitude balloon-borne hypsometric pressure gauge developed by Signal Corps Research and Development Laboratories. The standard radiosonde hypsometric pressure measurement device presently in use is accurate only at balloon altitude; in fact, there is some question of accuracy at balloon altitudes greater than 130,000 feet.

Tentative plans have been discussed relative to setting up a 10-station meteorological rocketsonde network in North America. Present plans call for the Arcas to be fired on a seasonal basis at 4 stations in North America beginning January 1960. The stations that are authorized are White Sands Missile Range, N. Mex.; Point Magu, Calif.; Fort Churchill, Man., Canada; and Wallops Island, Va. A series of 30 Arcas rockets will be fired at each of the above stations in January, April, July, and October. At present, only wind speed and direction and temperature will be measured. However, it is hoped that in later rocketsondes pressure measurements will be made. The above program is primarily supported by funds supplied by the Signal Corps Missile Geophysics Support Group based at the White Sands Missile Range, N. Mex. While the above network is being carried out by the White Sands Signal Corps, similar programs are being instituted by the Air Force Research Center at Cape Canaveral, Fla., and by the Signal Corps Research and Development Laboratories at Fort Greeley, Alaska, and Cape Canaveral, Fla.

The Cambridge Research Center firings are using a modified nose cone for measuring atmospheric density by means of a falling sphere. The payload for this series of flights consists of a 1-m.-diameter Mylar balloon packaged in a 40-cu.-inch cylinder welded into the Arcas nose cone. The parachute section of the basic rocketsonde system is eliminated, and the nose cone is mounted directly onto the rocket motor case. Separation of the package is accomplished by a modified Arcas separation device. Sufficient air is entrapped in the cylinder, which is sealed at sea level, to blow the end closure from the container and eject the balloon at high altitudes. The balloon is then inflated by means of a small amount of isopentane. Tests of the system have been successful, and a maximum altitude of 260,000 feet has been achieved.

The Signal Corps Arcas firings at Fort Greeley, Alaska, and Cape Canaveral, Fla. will use the modified AN/DMQ-6 in the nose-cone instrumentation package and the GMD-2 as the ground set. The 2 meteorological parameters that will be measured at Fort Greeley and Cape Canaveral are temperature and wind velocity.

The Ballistic Research Laboratories are interested in the Arcas rocketsonde for stratospheric research, primarily to measure water vapor, atomic oxygen, and other atmospheric constituents as shown in FIGURE 4.

FIGURE 5 shows the results of high-altitude balloon flights made

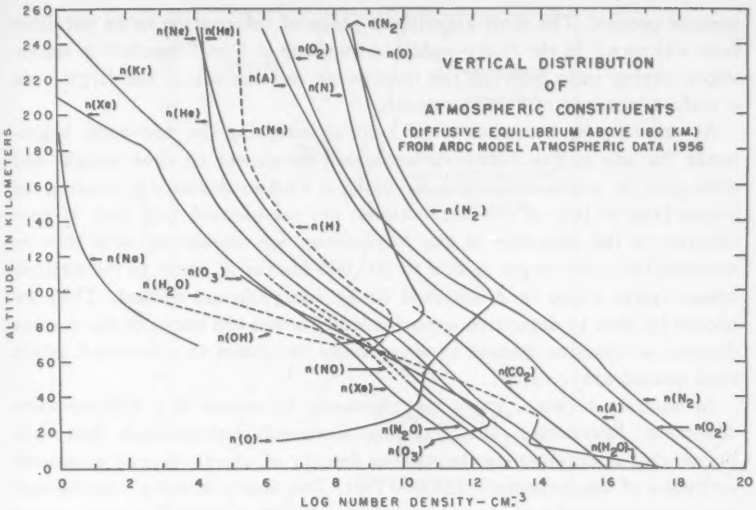

FIGURE 4. Vertical distribution of atmospheric constituents, 0 to 260 km.

at Fort Churchill, Man., Canada, in November 1958, and at Fort Monmouth, N. J., in April 1959. The purpose of the flights was to measure stratospheric water vapor in support of a Nike-Cajun high-altitude multiple-

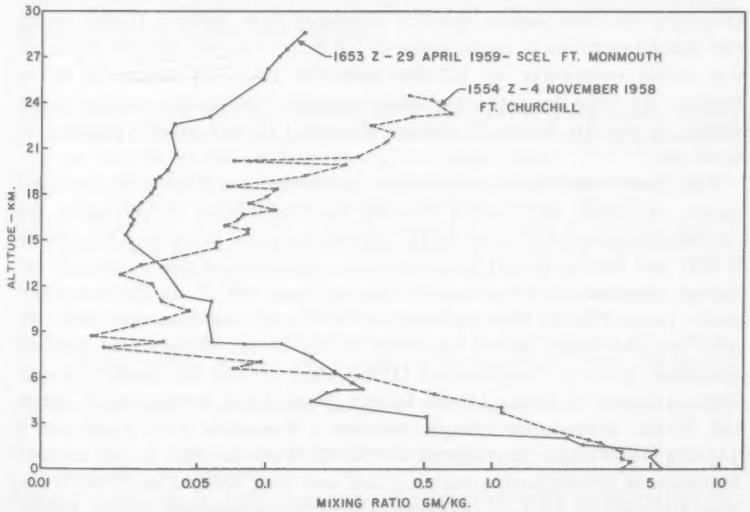

FIGURE 5. Vertical distribution of water vapor.

horizon project. The most significant piece of information to be obtained from FIGURE 5 is the thirty-eightfold increase at Fort Churchill in water-vapor mixing ratio between the tropopause and the top of the flight, and a sixfold increase at Fort Monmouth.

At present, my associates and I are redesigning the dew-point hygrometer for use in the Arcas rocketsonde. We expect to save weight and also gain in power efficiency by using a Peltier device for cooling the mirror face in lieu of the conventional dry ice-alcohol cold box. If successful in the redesign of the hygrometer, we should be able then to measure the water vapor profile to 200,000 feet or, at least, to the altitude where water vapor is diminished to an insignificant amount. Thus we should be able to determine experimentally where the curve of the number density or absolute amount of water vapor as shown in FIGURE 4 bends back toward lower values.

In addition to water vapor measurements by means of a balloon-borne dew-point hygrometer, the Ballistic Research Laboratories has been successful in determining the number density of atomic oxygen at balloon altitudes of approximately 125,000 feet. The above density measurement was accomplished by measuring the recombination rate of atomic oxygen by means of a nickel-coated surface. The nickel surface acts as third body in the recombination of 2 oxygen atoms in forming molecular oxygen. At the same time this recombination, being exothermic, gives off 117,000 calories for each gram molecular weight of O_2 formed. The temperature increase of this reaction above the ambient temperature is an indicator of the recombination rate or number density of atomic oxygen *in situ* (FIGURE 6). The number density computed from balloon flights using the above technique is in the order of 1.0 by 10^{11} atomic oxygen particles per cubic centimeter at 125,000 feet (38 km.). By means of Arcas flights, we hope to determine experimentally the atomic oxygen curve shown in the Air Force Cambridge Research Center graph (FIGURE 4) to 65 km.

The above-mentioned composition parameters together with measurements of ozone and carbon dioxide are considered to influence the temperature structure of the Arctic stratosphere. We know from Kochanski (1955) and Ohring (1958) that there is a variation of the middle stratosphere temperature in the Arctic, that is, from –80° C. in December and early January to as high as zero to –10° C. in late June and July. We also see somewhat lesser variation in the Soviet rocketsonde profiles presented by E. G. Shvidkovskii (1959). Here we see the monthly temperature changes at Heiss Island (Franz Josef Land Archipelago), where the 50-km. temperature change between a November 1957 flight and a January 1958 flight is as great as 50° C. This is most likely a manifestation of the explosive warming that was first noticed at 25 to 30 km. over Germany in 1951 by Scherhag. On further consulting Ohring (1958), Dobson (1946), Craig (1949, 1950 and 1957), Elsasser (1942), and Palmer

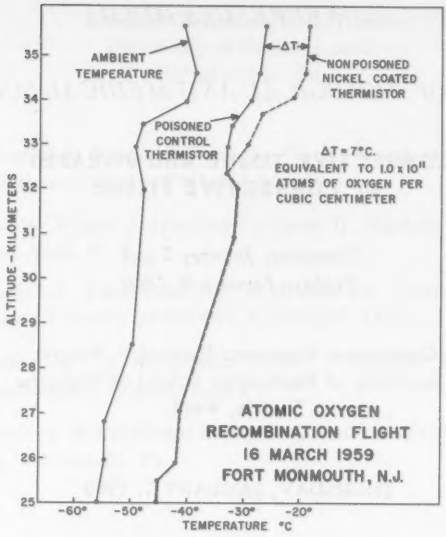

FIGURE 6. Vertical distribution of atomic oxygen.

(1959), we suggest that, in addition to the cutoff of solar radiation across the polar night, a substantial fraction of the temperature variation in the Arctic stratosphere is due to varying amounts of water vapor and ozone which, in turn, have an effect on the net gain or loss of infrared radiational energy in the Arctic stratosphere.

References

CRAIG, R. A. 1949. Radiative Heating and Cooling of the Ozone Layer, Special Report of Project on Establishment of a Solar Observatory Near Alamogordo, N. Mex. 39 pp. Harvard Univ. Press. Cambridge, Mass.

CRAIG, R. A. 1950. The observations and photochemistry of atmospheric ozone and their meteorological significance. Meteorol. Monogr. 1(2): 50.

CRAIG, R. A. & W. S. HERING. 1957. An explosive warming at 25 mb in January 1957. Tech. Mem. to Director, Geophys. Research Directorate. GRD-TM-57-17. Air Force Cambridge Research Center. Bedford, Mass.

DOBSON, G. M. B., A. W. BREWER, & B. CWILONG. 1946. Meteorology of the lower stratosphere. Proc. Roy. Soc. London. A 185: 144-175.

ELSASSER, W. M. 1942. Heat Transfer by Infrared Radiation in the Atmosphere. Harvard Meteor. Studies. No. 6., 107 pp. Harvard Univ. Press. Cambridge, Mass.

OHRING, G. 1958. The radiation budget of the stratosphere. J. Meteorol. 15: 440-451.

PALMER, C. E. 1959. The stratospheric polar vortex in winter. J. Geophys. Research. 64: 749-764.

SHVIDKOVSKII, E. G. 1959. Measurements of thermodynamic parameters of the stratosphere with aid of meterological rockets. J. Am. Rocket Soc. 29: 733-736.

CONFERENCES HELD

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

CONNECTIVE TISSUE AND DISEASES OF CONNECTIVE TISSUE

Thursday, January 7 and
Friday, January 8, 1960

Conference Chairman: Bernard M. Wagner
University of Washington School of Medicine
Seattle, Wash.

THURSDAY, JANUARY 7, 1960

Session Chairman: Jerome Gross
Harvard Medical School
Boston, Mass.

9:00 A.M.-
Greetings from the Academy - Robert L. Kroc, Chairman, Section of Biological and Medical Sciences, The New York Academy of Sciences, New York, N. Y.; Warner-Lambert Research Institute, Morris Plains, N. J.

Opening Remarks - Bernard M. Wagner, University of Washington, Seattle, Wash.

"Recent Studies in Protein Fibrogenesis" - David F. Waugh, Massachusetts Institute of Technology, Boston, Mass.

"Production of Mucopolysaccharides in Tissue Culture" - Charles Morris and Gabriel C. Godman, Columbia University College of Physicians and Surgeons, New York, N. Y.

"The Use of the Diffusion Chamber in Experimental Silicosis" - Robert C. Curran, St. Thomas's Hospital Medical School, London, England.

"Effect of Papain on Chondroitin Sulfate" - Robert T. McCluskey, New York University, New York, N. Y.

"The Chemistry of Wound Healing" - David Jackson and J. E. Dunphy, University of Oregon, Portland, Ore.

Session Chairman: T. N. Harris
University of Pennsylvania
Philadelphia, Pa.

2:00 P.M.-

"Cellular Basis of Antibody Formation" - S. Harris and T. N. Harris, University of Pennsylvania, Philadelphia, Pa.

"High Molecular Weight Antibodies" - Henry G. Kunkel, The Rockefeller Institute, New York, N. Y.

"The Concept of Autoantibodies in Rheumatic Fever" - Melvin H. Kaplan, Western Reserve University, Cleveland, Ohio.

"The Aschoff Body in Rheumatic Fever" - Bernard M. Wagner, University of Washington, Seattle, Wash.

"Immunopathology of Hypersensitivity" - Jacinto J. Vazquez, University of Pittsburgh, Pittsburgh, Pa.

FRIDAY, JANUARY 8, 1960

Session Chairman: William E. Ehrich
Graduate School of Medicine
University of Pennsylvania, Philadelphia, Pa.

9:00 A.M.-

"Amyloidosis: Clinical, Chemical, and Experimental Studies" - Evan Calkins, Alan S. Cohen, and Borge Larson, Massachusetts General Hospital, Boston, Mass.

"Electron Microscopic Studies of the Glomerulus in the Collagen Diseases" - Ben H. Spargo, University of Chicago, Chicago, Ill.

"Reactions to Homologous and Heterologous Fibrin Implants in Experimental Animals" - L. E. Glynn, Juvenile Rheumatism Research Unit, Taplow, Maidenhead, England.

"Parenchymal Fibrogenesis: The Liver" - Hans Popper, Mount Sinai Hospital, New York, N. Y.

"Immunochemical and Immunoelectrophoretic Studies of Patients with Agammaglobulinemia and Hypogammaglobulinemia - Occurrence of Connective Tissue Disease" - R. Bridges and R. A. Good, University of Minnesota, Minneapolis, Minn.

Session Chairman: Charles Ragan
Columbia University College of Physicians and Surgeons
New York, N. Y.

2:00 P.M.-

"Genetic Aspects of Connective Tissue Disease" - Victor A. McKusick, Johns Hopkins University, Baltimore, Md.

"Adrenal Cortical Function in Rheumatic Disease" - Vincent C. Kelley, University of Washington, Seattle, Wash.

"A Rational Approach to Therapy of Rheumatic Disease" - Joseph L. Hollander, University of Pennsylvania, Philadelphia, Pa.

PANEL DISCUSSION
TO SUMMARIZE THE CONFERENCE
SESSION CHAIRMEN AND SPEAKERS

Robert L. Kroc
Chairman

Charles Noback
Vice-Chairman

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES AND DIVISION OF MYCOLOGY

SECOND CONFERENCE ON MEDICAL MYCOLOGY

Monday, January 11 and
Tuesday, January 12, 1960

Conference Chairman: Chester W. Emmons
National Institutes of Health, Public Health Service
Bethesda, Md.

MONDAY, JANUARY 11, 1960

Session Chairman: Karl Maramorosch
The Rockefeller Institute
New York, N. Y.

GENERAL, NEW, AND EXPERIMENTAL MYCOSES

9:00 A.M. –
Greetings from the Academy – Robert L. Kroc, Chairman, Section of Biological and Medical Sciences, The New York Academy of Sciences, New York, N. Y.; Warner-Lambert Research Institute, Morris Plains, N. J.

Introductory Remarks – Karl Maramorosch, Chairman, Division of Mycology, The New York Academy of Sciences, New York, N. Y.; The Rockefeller Institute, New York, N. Y.

"Phycomycoses" – Lie-Kian-Joe, University of Indonesia, Djakarta, Indonesia.

"Growth Characteristics of the Fungi of Chromoblastomycosis" – Margarita Silva, Columbia University College of Physicians and Surgeons, New York, N. Y.

"Geographic Occurrence and Distribution of Mycoses" – Libero Ajello, Communicable Disease Center, Chamblee, Ga.

"The Effects of Cortisone on Experimental Mycoses" – Donald Louria, The New York Hospital-Cornell Medical Center, New York, N. Y.

"Experimental Dermatophytosis" – Albert M. Kligman, University of Pennsylvania Medical School, Philadelphia, Pa.

"Pathogenesis of 'Epidemic" Histoplasmosis" – Jan Schwarz, Jewish Hospital, Cincinnati, Ohio.

Session Chairman: Jan Schwarz
Jewish Hospital
Cincinnati, Ohio

EPIDEMIOLOGY, BIOCHEMISTRY, AND PHYSIOLOGY

2:00 P.M. –

"The Occurrence of Candida and Yeasts in the Intestinal Tracts of Animals" – N. van Uden, Instituto Botânico, Faculdade de Ciencias, Lisbon, Portugal.

"The Epidemiology of Dermatophytosis" – Lucille George, Communicable Disease Center, Chamblee, Ga.

"Histoplasmosis" – Howard W. Larsh, University of Oklahoma, Norman, Okla.

"Cryptococcosis" – Chester W. Emmons, National Institute of Allergy and Infectious Diseases, Public Health Service, Bethesda, Md.

"Physiology of *Coccidioides immitis*" – George W. Lones, National Institute of Allergy and Infectious Diseases, Public Health Service, Bethesda, Md.

"Approaches to the Physiology of *Coccidioides immitis*" – Demosthenes Pappagianis, University of California, Oakland, Calif.

"Mechanisms of Action of Antibiotics" – S. Gaylen Bradley, University of Minnesota, Minneapolis, Minn.

TUESDAY, JANUARY 12, 1960

Session Chairman: Albert M. Kligman
University of Pennsylvania Medical School
Philadelphia, Pa.

IMMUNOLOGY OF MYCOSES

9:00 A.M. –

"Some Aspects of the Mode of Action of Antifungal Antibiotics" – E. Drouhet, Institut Pasteur, Paris, France.

"Experimental Cryptococcosis" – Herbert F. Hasenclever, National Institute of Allergy and Infectious Diseases, Public Health Service, Bethesda, Md.

"The Accuracy of Serologic Methods of Diagnosis" – Charlotte Campbell, Walter Reed Medical Center, Washington, D. C.

"The Question of Immunity in Ringworm Infections" – Lorraine Friedman, Tulane University, New Orleans, La.

"The Capsule of Cryptococcus and Its Reaction with Antibody" – E. Edward Evans, University of Alabama Medical Center, Birmingham, Ala.

"Antigens of *Blastomyces*" – Stanley Marcus, University of Utah, Salt Lake City, Utah.

Session Chairman: Howard W. Larsh
University of Oklahoma
Norman, Okla.

THERAPY

2:00 P.M. –

"Experience with Amphotericin B" – John H. Seabury, Louisiana State University School of Medicine, New Orleans, La.

"Experience with Amphotericin B and Pimaricin" – Victor D. Newcomer, University of California Medical Center, Los Angeles, Calif.

"Griseofulvin" – Frank Roth, University of Miami Medical School, Miami, Fla.

"Griseofulvin in Systemic Mycoses" – Antonio Gonzales Ochoa, Instituto de Salubridad y Enfermedades Tropicales, Mexico City, D.F., Mexico.

"Nystatin" – Elizabeth Hazen and Rachel Brown, New York State Health Department, Albany, N. Y.

"Tennecetin" – Ashton Welch, Cincinnati, Ohio.

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

Robert L. Kroc
Chairman

Charles Noback
Vice-Chairman

DIVISION OF MYCOLOGY

Karl Maramorosch
Chairman

Emanuel Grunberg
Vice-Chairman

NEW MEMBERS

Elected January 28, 1960

LIFE MEMBERSHIP

Auditore, Joseph Vincent, Ph.D., Medical Research. Instructor, Pharmacology, Vanderbilt University, Nashville, Tenn.

Dodds, Wayne S., Ph.D., Chemical Engineering. Laboratory Director, General Foods Research Center, Tarrytown, N. Y.

Thrasner, George W., Ph.D., Animal Nutrition. Research Animal Nutritionist, Commercial Solvents Corporation, Terre Haute, Ind.

SUSTAINING MEMBERSHIP

Holzworth, Dorothy C., M.D., Bacteriology. Anesthesiology Staff, Maryland General Hospital, Baltimore, Md.

ACTIVE MEMBERSHIP

Acree, William B., M.D., Medicine. Private Practice, Ridgely, Tenn.

Ammon, Robert, Ph.D., Enzymes. Direktor des Physiologisch-Chemischen Institute der Universität des Saarlandes, Homburg-Saar, Germany.

Ang, Manuel, M.D., Circulation and Respiration. Research Fellowship, State University of New York, Brooklyn, N. Y.

Antonowich, Fred, M.D., Surgery. Surgical Resident, Grasslands Hospital, Valhalla, N. Y.

Apostol, Romeo Retes, M.D., Neurology and Neurochemistry. Assistant Professor, Neurology, University of the Philippines College of Medicine, Manila, Philippines.

Ashworth, C. T., M.D., Pathology. Professor and Chairman, University of Texas, Southwestern Medical School, Dallas, Texas.

Bacharach, Martin M., Ph.D., Biology. Assistant Director, Nutrition Research, Dawe's Laboratories, Inc., Chicago, Ill.

Bailey, W. S., Sc.D., Veterinary Medicine. Head Professor, Department of Pathology and Parasitology, Auburn University, Auburn, Ala.

Barkin, Stanley M., Ph.D., Physical Polymer Chemistry. Research Chemist, Ethicon Inc.. Somerville, N. J.

Barlow, Joan, M.N., Medicine. Editor, Squibb Nurse Notes, New York, N. Y.

Barnhart, Marion I., Ph.D., Cellular Physiology. Associate Professor, Wayne State University, College of Medicine, Detroit, Mich.

Belle, Martin S., M.D., Cardiovascular Diseases. Assistant Clinical Professor of Medicine, University of Miami Medical School, Miami, Fla.

Bengtson, John W., B.Sc., Internal Medicine. Lincoln Clinic, Lincoln, Nebr.

Benjamin, Harry, M.D., Gerontology. Private Practice, New York, N. Y.

Berman, David, M.D., Medicine. Private Practice, Charlestown, Mass.

Black, Boyd K., M.D., Pathology. Director of Laboratories, Good Samaritan Hospital, Vincennes, Ind.

Blaker, Robert G., Ph.D., Medical Microbiology. Instructor, Woman's Medical College of Pennsylvania, Philadelphia, Pa.

Blosen, Rosemarie, M.D., Anesthesiology. Private Practice, Waterloo, Iowa.

Blumenfeld, Margaret, M.D., Anesthesiology. Assistant Professor, State University of New York, College of Medicine, Brooklyn, N. Y.

Blye, Richard Perry, Ph.D., Endocrinology of Reproduction. Associate Scientist, Ortho Research Foundation, Raritan, N. J.

Bobb, Yvonne Dolores, Ph.D., Immunology. Research Associate, Palo Alto Medical Research Foundation, Palo Alto, Calif.

Bock, Fred G., Ph.D., Biochemistry. Associate Cancer Research Scientist, Roswell Park Memorial Institute, Springville, N. Y.

Bodi, Tibor, M.D., Clinical Pharmacology. Associate in Medicine, Department of Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pa.

Bogedain, William, M.D., Chest Surgery. Thoracic Surgeon, Timken Mercy Hospital, Canton, Ohio.

Bois, Gilles, D.C., Anatomy. Chiropractor, Private Practice, Montreal, Que., Canada.

Borchardt, Paul R., M.D., Medicine and Biology. Private Practice, Bronx, N. Y.

Bornstein, Bernard, M.D., Neurology. Associate Clinical Professor, Hebrew University, Jerusalem, Israel.

Boschetti, Armando, B.S., Pharmaceutical Research. Assistant Director of Research, SchenLabs Pharmaceuticals Inc., New York, N. Y.

Box, Harold C., Ph.D., Physics. Research Scientist, Roswell Park Memorial Institute, Buffalo, N. Y.

Brahen, Leonard S., Ph.D., Medicine. Associate Director, Clinical Research, Chas. Pfizer & Co., Brooklyn, N. Y.

Brest, Albert N., M.D., Internal Medicine. Instructor, Hahnemann Medical College, Philadelphia, Pa.

Brown, Eric R., Ph.D., Immunochemistry. Associate Research Scientist, Chas. Pfizer & Co., Terre Haute, Ind.

Buddecke, Echart, M.D., Biochemistry of Connective Tissue. Research Fellow, Bellevue Medical Center, New York, N. Y.

Buñag, Ruben D., M.D., Pharmacodynamics. Associate Professor, Pharmacology, UE-RM Memorial Medical Center, Quezon City, Philippines.

Bush, Milton T., Ph.D., Pharmacology. Associate Professor, Pharmacology, Vanderbilt University School of Medicine, Nashville, Tenn.

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